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THE AMERICAN
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VOL. 96. JULY, 1924. NO. 7.

EDITORIAL

FRINGING THE HINTERLAND OF SCIENCE.

The outstanding theme of this hectic age is the speculation concerning the depletion of its known storehouses of energy. The whirling progress of the present, so alarmists state, is consuming its capital of resources. The world is being impoverished and posterity embarrassed by the lavishness of the current generation, in its expenditure of coal and petroleum residues.

To the scientist however, this gives but little concern. He knows that posterity will not be long embarrassed, for with the insight already gained into energy changes of reacting chemicals, and the possibilities of growing our motive fuel as we grow our body food fuel—new sources of energy will have been found long before our natural resources shall have been exhausted. Posterity with its scientific inheritance can well grapple with its own problems. In this as in all things—"sufficient unto the day its own troubles."

Nor do we ignore in this connection the need for conservation born not out of denial, but out of a careful nursing of our present stocks. Let the wheels of progress not stop, but rather proceed unhindered with watchful expenditure of its available energy stores. Chemistry leads the way, and the way of chemistry is neither wasteful nor unmindful of tomorrow.

In England after Waterloo, all good Englishmen planted acorns so that Brittania might ever rule the waves and never lack for sturdy oak wherewith to build her battleships. It was an idea consummated in pure loyalty, but it bespoke no real vision. For the Englishman builds his battleships today with bands of steel—and his oaks are only fashioned for his coffin.

Concern over the exhaustion of our natural fuel resources is just as unseemly and irrational as the oak planting notion. Of course conservation is wise and necessary—but there is no need for extravagant alarm in this direction. Dr. Slosson, author of that marvelous book "Creative Chemistry," in his inimitable style handles a prophecy of other fuels in this manner.

> "But our supply of petroleum will sometime run short, in a dozen or fifteen years at the present rate of consumption, according to the estimates of the oil in the ground by the U. S. Geological Survey. Sooner or later at any rate we must grow our fuel, as we grow our food, from year to year. It is interesting now to recall the prophecy of Dr. Diesel, shortly before his mysterious disappearance from the night boat that was carrying him from Germany to England just before the war. He foresaw the time when mineral oil would be exhausted, and then, he said, the supremacy of the sea would go to that power which possessed the most tropical territory for growing vegetable oil. Dr. Diesel has been dead but ten years, yet already in Africa boats are run with palm, cottonseed, and peanut oils. Diesel engines are reported to run on less than ten ounces of cottonseed oil per British horsepower-hour at a thermal efficiency of 24.5 per cent."

And growing our fuel is not nearly as impractical as it seems. We grow a great deal of it as it is. Take the production of alcohol for instance. A little active seed is planted. Out of the earth and out of the sun-flooded ether the little seedling draws its sustaining energy—and binding the energy in its make-up it grows to full maturity. Man cuts it down, soaks it in water awhile, and through the agency of an added yeast cell, or acid hydrolysis and ferment, changes its cellulose or starch to sugar and thence to alcohol. The energy bound by the plant is now contained in the alcohol, whence it can be promptly utilized when needed. In alcohol there is great promise as a fuel, for the forces that the little seedling drew out of the earth and out of the sunlit ether, are now locked in the atomic embrace of fluid alcohol, only awaiting an opportunity to work. One only has to imbibe a portion of it to know its availability in this direction.

It is in the integral forces of the inner atom however, that man may some day find his greatest fund of energy. The physico-chemical studies of radium and radium emanations are still very in-

complete, but we know that compressed into the atoms of this amazing element is a measureless amount of electronic action.

Some day perhaps, this and other similar forces, such as harnessed sunlight, will be strong in the service of man—whirling the buzzing wheels of industry—changing night to day—mounting the dizzy avenues of air and coursing steady through the lanes of ocean commerce.

Harnessed sunlight indeed is not an idle speculation. For recorders of scientific thought have often expressed such a possibility. Quoting again the words of Dr. Slosson, his statement seems far from a phantasy.

> "Still, the sun, sole source of all our life and weather, floods half the earth with its rays, and the land that receives the most of this potential wealth is the land that retains the least of it, the arid region of the tropics. A section of the Sahara, forty miles square, receives in six hours a day as much heat as is produced by the coal burned in the twenty-four hours throughout the world. If only a small fraction of this wasted energy could be economically stored up and set at work by some sort of solar engine, we need not worry about the exhaustion of our oil, gas and coal. There would be wealth enough for all."

Man indeed has but recently come to peer beyond the bounding fringes of chemical possibilities—and only then because of forced interest. The transient modes of life—the swiftly changing problems of his earthly tenantry have thrust him more and more to the ultimate study of this inexhaustible science. And as scurrying time builds up its scheme of centuries man will continue to extract from this prolific source wonders and wonders that shall reach beyond his wildest expectation.

"Yet all these were, when no Man did them know,
Yet have from wisest Ages hidden beene;
And later Times things more unknown shall show.
Why then should witlesse Man so much misweene,
That nothing is, but that which he hath seene."

Ivor Griffith.

SOME ASPECTS OF THE ALCOHOL PROBLEM.

Hermann C. Lythgoe, Director of the Food and Drug Division of the Massachusetts Department of Health, made an address before the New England Health Institute at Boston on May 5 last, which has been published in the *Chemical Age* (1924, *32*, May issue.) Lythgoe is well known in the field of food and drug analysis, and has had a long and important experience with all phases of the subject. He has had especially active work in connection with the examination of intoxicating beverages in the last few years. In earlier years about 100 samples per year were submitted for examination, but in 1921 the number rose to 3831, and in 1923 to 6367. The work is increasing in a rapid ratio; 6841 samples have already been submitted up to April 30, 1924.

With such figures before us, we may well ask what amount of so-called "poison rum" has been found. The answer would appear to be that scarcely anything known to be definitely poisonous except ethyl alcohol has been detected. In the newspaper literature of the present day, "poison-rum" is a mere shibboleth, but one cannot expect newspapers to care anything for exact science. In scientific literature, however, there appears to be an effort to impress the community with the view that there is something in illicitly distilled liquors which is specifically poisonous. Attention was called a few months ago in this journal to reports by Doran and Beyer of examination of very many samples of illicit liquors, in which report attempts were made to charge excess of aldehyde as a cause of unwholesomeness. This claim will not stand cross-examination. There are no clinical or experimental data showing that minute amounts of acetaldehyde, such as occur in even illicit liquors are injurious. This aldehyde is a constant and notable ingredient of fresh apple juice. Chemists and physicians who talk about "poison rum" as being due to the accessories of the fermentation will do well to note what Lythgoe says in his address. Referring to the fact that Crampton and Tolman in their thorough and classical investigation found that none of accessories were reduced in absolute amount by long storage and were increased in proportion to the alcohol on account of the evaporation of the latter, Lythgoe says:

"If these secondary bodies are the cause of the untoward symptoms of alcoholism, 'hooch' should be safer to drink than aged liquor. It is possible that these secondary bodies may act as negative catalysts, but then again they may not. As stated by Adams (*J. I. E. C.*, 1910, *2*, 34) in his publication upon the distillation of whiskey, the substances which produce the unpleasant odors frequently found in the tail of the distillation are not fusel oil, as commonly supposed, but factors at present undeterminable, probably being water-soluble products of fermentation, distilled over from the beer. The probable result of ageing is the production of agreeably-smelling bodies, which act as counter stinks, thereby making the ingestion of the intoxicant a more agreeable pastime."

In the Massachusetts experience great increase in the retail sales of tincture ginger has been noted. This consumption has been quite out of proportion to the requirements for gastric disturbances, and, similarly, the sales of rubbing alcohol have been far in excess of the needs for sprains and other applications. There is no reason to doubt that much manipulation of these preparations is going on. The allusion in the United States regulations to the method by which an alcohol containing diethyl phthalate can be deprived of that ingredient offers a good opportunity for utilizing one of most familiar forms of rubbing alcohol.

In my opinion the time has come for physicians and chemists to take a decided stand before the public to the effect that the poisonous ingredient in alcoholic beverages is ethyl alcohol. How any one can doubt this and further try to lay blame on accessory ingredients which are not diminished appreciably by long ageing and have not been shown to be more toxic than alcohol itself, passes my understanding. The most absurd view seems to be the statement that acetaldehyde is a specific cause of poisonous action. It is present in almost all fermented beverages, and is in notable amount in fresh apple juice. To charge it with a specific action in cases of alcoholism is to ignore all the data accumulated on the subject.

HENRY LEFFMANN.

PHARMACISTS' ASTHMA.

About a quarter of a century ago Professor Richet, of Paris, found that the injection of foreign proteins into certain animals, notably the guinea pig, produced an extreme sensitiveness to the same protein, so that very minute quantities of a substance which had previously been given without any demonstrable injury would, on the second dose, produce serious symptoms and even fatal results. For this artificially begotten sensitiveness he suggested the term anaphylaxis. Later evidence was brought forward to show that certain diseases of obscure origin were due to an extraordinary individual susceptibility towards substances which are practically non-toxic for the mass of humanity; the two conditions of this type which have received the most attention are asthma and hay fever. This susceptibilitiy to certain foreign proteins is not properly speaking anaphylaxis, although it is probably an allied condition. To it the term "allergic" is generally applied.

These idiosyncrasies are most remarkable and have received within the last few years much attention from the medical profession. The causative relation of the pollen of various plants to hay fever is well established and in recent years the proteins of various foodstuffs have been prepared for testing allergic sensitivity.

In the *Journal of the American Medical Association* for June 7, 1924, Dr. M. M. Peshkin has published an account of allergic manifestations* occurring among pharmacists. One large manufacturer states that they have had upwards of one hundred cases yearly of patients "suffering from bronchial asthma or other evidences of respiratory irritation from dust, chiefly resulting from grinding ipecac." Two firms reported that they had had to transfer several persons from the milling and grinding room on account of their sensitiveness to certain powders. The drugs that they have found to cause these disturbances in order of the frequency of their deleterious action, include ipecac, podophyllum, pokeroot, lycopodium and rhubarb. In addition, handling of vanilla beans and emetine solutions caused irritations of the skin

*Reprinted on page 524 of this Journal.

which are evidently allied to these allergic symptoms. Bernton (*American Journal of Medical Science*, 1923, p. 196) reported also a case of sensitization to the castor bean. It is not determinable with certainty whether these idiosyncrasies are congenital or whether they are a true anaphylaxis, that is—an acquired sensitiveness developed from previous exposure.

Whether or not it is possible to desensitize these individuals by the use of gradually increasing doses of the offending substance, as is done with certain food proteins, has apparently not been studied. The cases reported were satisfied with the relief of avoiding contact with the drug to which they were sensitive. Dr. Peshkin believes that cases of this type among the pharmacists are probably more common than is generally supposed.

HORATIO C. WOOD, M. D.

ORIGINAL ARTICLES

THE DEVELOPMENT, PHARMACOLOGY AND RELATIVE TOXICITY OF THE MODERN LOCAL ANESTHETICS.*

By Charles W. Hooper, A. B., M. D.

Local anesthetics are administered to millions of individuals every year, and for this reason, if for no other, the pharmacist should thoroughly acquaint himself with the pharmacology, relative toxicity and practical uses of the various drugs that are used as local anesthetics.

Doctor P. G. Skillern, Jr., 1922, Associate Professor of Surgery, University of Pennsylvania, compares modern local anesthesia and general anesthesia in the following words:

> "In the drift of present-day thought and action among the laity there is evidence of increasing appreciation of what constitutes the best service surgery has to offer, for nowadays we find that people are coming to us demanding local anesthesia for their operations. Especially is this true of those who have previously taken a general anesthetic, and of those who have

*Address to the students of the Philadelphia College of Pharmacy and Science, April 15, 1924.

had a friend operated upon under local anesthesia. The reason for this demand is easily understood, for everyone carries with him a subconscious dread of a surgical operation—a dread engendered by the belief held for thousands of years that it is a terrible ordeal. In truth, previous to the days of ether anesthesia a surgical operation was a terrible ordeal; but even now many patients put off their operation from dread of ether and the fear that they may never 'come out' of it. And when there is a deeply-rooted conviction there is usually a pretty good basis for it.

"Statistics recently collected by Salzer and Stewart give the mortality rate from general anesthesia as 1 in 600. Every practicing physician has seen patients die of ether shock, or ether toxemia terminating in post-anesthesia pneumonia, fibrillation of the heart and acute dilatation, thrombosis with embolism, acute dilatation of the stomach, paralytic ileus, acidosis, etc.—all instances of the evil effects of a general anesthetic, but not one the result of the surgery. But even in the case of the usually successful and safe administration of ether it is no pleasant sight for the relatives to behold their beloved one unconscious, tossing about and vomiting after operation; and how they rejoice when the patient is able to give them the first sign of recognition! And there are yet to be endured the craving for water, the distressing gas pains of the first twenty-four hours, and on the part of the medical attendant the anxiety during convalescence lest one of the above-mentioned delayed ether complications should ensue.

"On the other hand, patients are learning that when operated upon under local anesthesia they are spared practically all these discomforts or disasters that attend the use of ether. Most people prefer to remain awake and conscious during an operation in which they will have no pain. Many operations under local anesthesia are no more of an ordeal than getting a haircut or a shave; often the patient scarcely need to go to bed after operation. After all, the appeal of local anesthesia to the public is intimately connected with their primal instinct of self-preservation.

"Now there is another—a very personal—reason why patients fare better under local anesthesia, to wit: By it a surgeon is going to safeguard the patient against crude, rough and clumsy work on the part of the operator; the corollary of which is that local anesthesia exerts a refining influence upon the operator's technic, so that he develops precision, neatness and skill and learns a wholesome respect for tissues, with the result that operative trauma is reduced to the minimum. And the operator using local anesthesia dare not work against the clock, but must work slowly and carefully. But since with local anesthesia there is by no means the risk that attends a

prolonged ether anesthesia, time is not a factor, and therefore more careful attention can be devoted to details of technic. The consensus today among doctors—and often among the laity—is that when undergoing operation except in emergencies they want plenty of time devoted to the making of a thorough job. A good illustration is the hernia operation, which, in order to insure against recurrence, must be done painstakingly and with great deliberation. For a surgeon to use local anesthesia, therefore, is a question of his being willing to take the additional time and care, exert the additional mental effort, and undergo the greater strain.

"While ether is a treacherous anesthetic in those who apparently are physically fit subjects for it, it is extremely hazardous to administer it to those whose vital functions are impaired or wrecked by acute or chronic disease. Certain operations may be performed under local anesthesia with perfect safety upon patients who would have died under general anesthesia. In this category belong, first, those patients of advanced age; second, those with handicapped cardiac, respiratory, hepatic or renal organs; third, those with altered metabolism, toxemia, acidosis, 'status lymphaticus.'

"A not unimportant advantage of local anesthesia is its safety. In a paper entitled 'The Causes of Our Post-Operative Deaths,' based upon a review of 1430 operations performed at Tonsberg's Hospital, Norway, Paus and Lorange recommend, as the means of diminishing the number of post-operative deaths, the extended use of local anesthesia. Bartlett states that by using it with correct technic one may be practically sure that he creates no immediate danger to life. Of the drugs employed, novocain is thoroughly effective and the safest of local anesthetics available today. Not only is novocain the safest local anesthetic, but it is generally acknowledged to be the safest of all known anesthetics. If properly administered, novocain may be used almost *ad libitum*, for extended experience of many clinicians shows that in the case of the ordinary adult 200, 300 or even 500 cc. of a 0.5 per cent. solution is safe.

"The future of local anesthesia is well forecast by Bartlett, who believes that with increasing experience and better training we shall some day have to establish indications for general anesthesia, rather than for local, as is the common experience today; it will then seem no more reasonable to anesthetize the entire organism for a strictly local operation on it, than it would be at the present time to bind or splint the entire body for an injury to an extremity. I, too, feel that the demonstrated and acknowledged lower post-operative morbidity and mortality with local anesthesia will eventually force a widespread adoption of this method."

Pharmacologically, the general anesthetics are chemical substances, known as hypnotics, which act directly on the brain and spinal cord, inhibiting its function while leaving the sympathetic centers of respiration and circulation comparatively unaffected. Ether, ethyl chlorid, chloroform, nitrous oxid, and other substances, when properly administered, produce a sensory depression and general unconsciousness by direct action on the central nervous system. This is called narcosis or general anesthesia. The disadvantages of general anesthesia lie in the fact that it affects the entire organism and not only a circumscribed portion; that a certain number of fatalities are inevitable; that its induction is usually followed by unpleasant after-effects, and that it requires trained assistants and considerable technical detail for administration.

Dr. Emil Mayer's Committee on Local Anesthesia, 1920, states that local anesthesia is the method of choice by practically all American rhinologists, and for throat operations the majority operate under local anesthesia and declare themselves to be entirely content with it. There is less hemorrhage, far greater safety, and the dangers of toxicity compare favorably in the use of the local anesthetic in preference to any general anesthetic. They further state that even the nitrous oxid and oxygen combination, looked on by many as absolutely safe, has a record of deaths that destroys that assuredness. One observer has reported thirty-seven deaths from this "safest" anesthetic.

McCormick, 1923, collected 163 deaths in the United States due to nitrous oxid.

Braun, 1922, states that in 50 per cent. of all surgical operations local anesthesia can successfully replace general anesthesia.

Modern local anesthesia, as distinct from general anesthesia, is produced by the application of certain chemical substances directly on the operative field, which act electively on the nerve tissues in a circumscribed area. It is based upon the possibility of temporarily inhibiting the conductivity of the sensory nerve endings without causing permanent tissue injury. This result can be obtained by certain chemical substances in two ways, either by acting directly on the nerve terminals, called terminal or infiltration anesthesia, or by acting on the nerve trunks supplying the site of operation, thereby interrupting the conduction of sensory impulses. This we call regional or conduction anesthesia. Both methods are capable of wide and effective application.

The introduction of the hypodermic syringe in 1853 by Alexander Wood made possible local anesthesia through the pharmacologic action of special drugs. Wood immediately began to inject morphin in the neighborhood of nerve trunks for the relief of neuralgia. Success was reported, but the relief was due no doubt to the systemic action of morphin rather than to its local action. Many other drugs were thus tried, but with no success until the discovery of the use of cocain in 1884 by Karl Koller of New York. This discovery, following thirty years after the introduction of the hypodermic syringe, marks the beginning of the modern development of local anesthesia. Today local anesthesia is of great importance in surgery and is employed by thousands of surgeons and the majority of dentists. The alkaloid cocain, for over twenty years the only local anesthetic, has gradually fallen into disuse as a local anesthetic. It is now regarded as a very dangerous drug. Surgeons who still employ cocain restrict its use to topical applications and state that it should never be injected beneath the skin. Although cocain has been superseded, it was the first of the modern local anesthetics and so deserves prior consideration.

Cocain.

The coca plant (*Erythroxylon coca* Lam.) is a shrub native to tropical South America, especially Peru and Bolivia. From time immemorial it has been prominent in the religious and political lives of the people. The interest of the scientific world was first aroused by the reports of travelling investigators who discovered that the coca leaves were chewed by the natives of South America in order to alleviate hunger, to produce wakefulness, and to increase their physical powers of endurance. The alkaloid cocain was first isolated from coca leaves in 1860 by Woehler, who, in his original publication, noted that it had a peculiar numbing effect on the tongue, making the spot it had touched temporarily quite insensitive. Twenty-five years elapsed before the practical value of this observation was recognized, when Koller first published his researches.

Cocain is a crystalline substance sparingly soluble in water. It combines readily with acids to form salts, of which the hydrochloride is the best known, and the most frequently used therapeutically. Cocain hydrochloride is a white crystalline powder which is readily soluble in water and alcohol. It is known chemically as benzoyl-methyl-ecgonin hydrochloride.

Water solutions of cocain are not very stable and are frequently contaminated by the growth of molds. Long-continued boiling decomposes cocain into benzoyl-ecgonin and methyl alcohol. A single rapid boiling of a small quantity of water solution is not followed by a material loss of cocain, whereas the repeated boiling of large quantities of the solution, or sterilization in an autoclave, causes a diminution in the cocain content with a diminished activity of the solution.

As stated above, successful local anesthesia made its first important advance in 1884 when Koller introduced cocain as a modern local anesthetic. He demonstrated that by the instillation of a 2 per cent. cocain solution the eye could be made sufficiently insensitive to carry out many operations without pain. Koller's discovery soon proved of great value in laryngology and rhinology where operations could be more exactly performed than with general anesthesia. Within the next few years the use of cocain was common in all branches of surgery. It was employed for terminal or infiltration anesthesia to anesthetize the terminal nerves in the field of operation, for regional, conduction or block anesthesia by injecting the solution into and around nerve trunks; and finally for intraspinal anesthesia, by injecting the solution directly into the spinal canal.

The rapid progress made in local anesthesia soon met with almost insurmountable difficulties. Mild, severe and fatal cases of cocain poisoning were observed in great numbers. Cocain poisoning, the habit-forming property of the drug, the instability of its solutions, as well as fluctuating supplies and high cost, led to intensive chemical study with a view to discovering other substances which would be equally efficient as local anesthetics without the serious defects of cocain. The success of these endeavors is attested by the extremely restricted use of cocain at the present time.

The first step in the development of the newer types of local anesthetics was the determination of the chemical structure of cocain. This was accomplished by the researches of Lieberman, Willstaetter, and particularly by Einhorn. It was found that the anesthetic property of cocain depended upon the esterification of a basic alcohol, methyl-ecgonin, with benzoic acid, and after many years of study in this field, starting from this observation, Einhorn stated the definite principle that all esters of aromatic acids produce a greater or lesser degree of local anesthesia. As a result, many alkamine esters of aromatic acids have been discovered which have

the properties of a local anesthetic. Among those introduced into practice may be mentioned tropacocain, beta eucain, stovain, alypin, novocain, apothesine and butyn. Novocain, the least toxic of this entire group, was prepared by Einhorn in 1903.

A number of other types of substances have been investigated as local anesthetics: Holocain, a phenetidin derivative used in ophthalmology; chloretone, a number of phenols, vanillin, saponin and many other substances. Macht in 1918 called attention to the anesthetic properties of benzyl alcohol. Hirschfelder, 1920, investigated the anesthetic action of other aromatic alcohols and states that out of this series saligenin or salicyl alcohol is the best and least irritating.

A group of benzoic acid derivatives, insoluble in water, namely, the alkyl esters of amido-oxy-benzoic acids and the alkyl esters of amido-benzoic acids, have also been described, which possess more or less strong anesthetizing properties when in direct contact with exposed nerve ends. They contain no basic group which is capable of forming neutral water-soluble salts. Owing to their insolubility in water and tissue fluids they cannot penetrate the intact skin or mucous membrane and they cannot be used in surgery where a water solution of the drug is to be injected into the tissues. The use of these compounds has therefore been limited to direct application to wounds, ulcers, burns, excoriations, etc., where there may be exposed nerve ends. The amido-oxy-benzoic acid esters were developed by Einhorn, who prepared more than forty different esters, all of which showed anesthetic properties. From this series orthoform, the methyl ester of m-amido-p-oxy-benzoic acid, was introduced into practice. Of the p-amido-benzoic acid series anesthesin or parathesin, the ethyl ester, is the best known. Many other esters have been made and their possible number is limited only by the number of alcohols which can be esterified.

Novocain.[1]

Novocain was introduced into the practice of medicine by Professor Braun in 1905. It fulfilled his requirements for a cocain substitute in a very exact manner. Since the introduction of novo-

[1] Procaine is the name, decided upon by the U. S. Federal Trade Commission, for this anæsthetic compound. Novocain is a brand of procaine manufacture by H. A. Metz Laboratories, Inc., New York, by license from the Commission. (Note by Editor.)

cain an extremely large number of surgeons and dentists have demonstrated the unique value of this local anesthetic. The Committee on Synthetic Drugs of the National Research Council included novocain among the three most necessary synthetic drugs. The rapid extension of its employment and the fact that nineteen years after introduction it has found its way into every important clinic and has in general use practically superseded all other soluble local anesthetics for infiltration, conduction and intraspinal anesthesia, is a sufficient testimonial of its value in therapy.

Novocain is a white crystalline substance which can be heated to 120 degrees C. without decomposition. It dissolves in equal parts of cold water, the solution giving a neutral reaction. Water solutions can be sterilized by boiling or autoclaving without deterioration, and can be kept in stoppered flasks almost indefinitely without change in color. It has no irritating qualities when applied in concentrated solution (20 per cent.) upon fresh wounds. When instilled into the eye it causes no disturbance and even when the pure drug is sprinkled on the cornea it causes only slight irritation of short duration. The infiltration of tissues with novocain solution (0.5 per cent. to 2 per cent.) causes no vaso-constriction or vasodilatation and leaves no after-effects upon the tissues.

Novocain solution when injected subcutaneously exerts the same action upon the peripheral sensory nerves as cocain and when combined with epinephrin it produces as pronounced and as lasting anesthesia. It may be combined with suprarenin, a synthetic product identical with the active principle of the adrenal gland, the combination producing rapid and prolonged anesthesia with temporary ischemia of the anesthetized tissues.

It is not a habit-forming drug and its sale and distribution are not governed by the Harrison Anti-Narcotic Act.

A number of attempts have been made to simplify the clinical use of novocain. Accordingly, Braun introduced novocain tablets of definite weight, with and without combination with suprarenin. These tablets are intended to avoid the necessity of weighing out the novocain and to facilitate the preparation of small amounts of solution. They have come into extended use for minor operative procedures, particularly in the field of dentistry.

The question of having ampules made by the manufacturer containing ready-prepared solutions of the synthetic local anesthetics has been favorably considered by the Committee of the American Medical Association on Local Anesthetics. Ready-to-use

solutions of novocain are now available in various dilutions and quantities, with and without the addition of suprarenin. These water-clear solutions are sterile, stable and very efficient.

Sealed glass ampules are also being manufactured containing concentrated sterile novocain and novocain-suprarenin solutions. These are a great convenience to the surgeon and afford protection against avoidable accidents and mistakes in the preparation of such solutions. Ampules of this type place novocain in the hands of the surgeon so that a sterile, fresh, dilute novocain solution of the desired strength can be prepared immediately at the time of operation by simply adding the contents of one ampule to a known volume of physiologic salt solution at hand in the operating room. Such a procedure assures the surgeon that he is not using a 20 per cent. stock novocain solution or a novocain solution prepared with saturated salt solution. The suprarenin is contained in the ampule in order to eliminate the chance of adding an epinephrin solution which is not sterile or one which has deteriorated.

Experimentally there is no drug used in medicine which has been subjected to more exhaustive or more critical pharmacological investigation. Foremost among the investigators may be mentioned Biberfeld, 1905; Le Brocq, 1909; Piquand and Dreyfus, 1910; Frankfurther and Hirschfeld, 1910; Hatcher and Eggleston, 1916; Roth, 1917, and Eggleston and Hatcher, 1919. All are agreed that novocain is less toxic than cocain or any of the alkamine esters of aromatic acids which have been introduced as substitutes. The results of the experiments of Eggleston and Hatcher, 1919, show that the amount of novocain required by intravenous injection to cause death in experimental animals varies very widely with the rate of administration, and that enormous amounts can be injected slowly without causing death.

For a given animal, all experimental factors being equal, the great difference in the toxicity of novocain and cocain is caused by the difference in the rate of elimination of the two drugs. Novocain is rapidly eliminated by destruction in the liver. Cocain is slowly excreted, mainly through the urine. Eggleston and Hatcher, 1919, have shown that by slow or repeated intravenous injection the cat's liver can detoxify or destroy novocain at the rate of at least one rapidly injected fatal vein dose every twenty minutes. Cocain, on the other hand, is eliminated so slowly that the animal soon develops symptoms of cumulation, as shown by the increasing severity of the symptoms and its ultimate death.

Hatcher and Eggleston, 1916, demonstrated a certain antagonism between novocain and epinephrin. The simultaneous intravenous injection of small effective doses of the two drugs causes a rise in blood pressure, higher and more sustained than after a similar dose of epinephrin alone. Novocain alone in similar dose caused a fall in blood pressure.

Accurately controlled animal experiments showing the relative toxicity of the various drugs used as local anesthetics have a direct clinical application in supplying unbiased data by which the relative safety of the drugs may be estimated.

Professors Hatcher and Eggleston, 1919, were the first to carry out comprehensive experimental work to determine the relative toxicity of all of the drugs used as local anesthetics. They realized that the toxic action of the local anesthetics is exerted only after the entrance of the drugs into the blood stream and therefore that the most accurate method of determining the relative toxicity of the local anesthetics is to determine the maximal toxicity of each after intravenous administration. They determined the maximal toxicity of each by rapid intravenous injection of water solutions of the drugs into cats. The concentration of the solutions varied from 1 to 20 per cent., so that the dose could be injected from a syringe in from five to fifteen seconds.

In view of the fact that the ratio of toxicity of each of the local anesthetics varies greatly in different species of animals when injected subcutaneously, Miss Becker and I, 1924, decided to determine the maximal toxicity by intravenous injection in some species other than the cat and also to see if we could develop a method which from an experimental viewpoint might be considered quantitative. For this purpose we adopted a test based upon the official method used by the Hygienic Laboratory, United States Public Health Service, and the manufacturers to determine the toxicity of the salvarsans before they are released for distribution. The Government selected the rat for this test because the results obtained seemed to be more constant than with other experimental animals. Furthermore, on account of their small size, a large number of rats can be kept conveniently under uniform conditions of diet, weight, etc., and as a result more animals can be used for an individual test.

We have applied a modification of the official technique for the determination of the maximal toxicity of the alkamine esters of the aromatic acids used as local anesthetics and have found that

the results obtained are very accurate and correspond very closely to those obtained with the cat by Professors Hatcher and Eggleston.

The chart is based upon results obtained with over 300 albino rats. A 2 per cent. solution of the drug in distilled water was injected into the saphenous vein at the rate of twelve to fifteen seconds for every 0.1 cc. At least five animals were injected at each dose. The minimal dose at which any of a series of animals

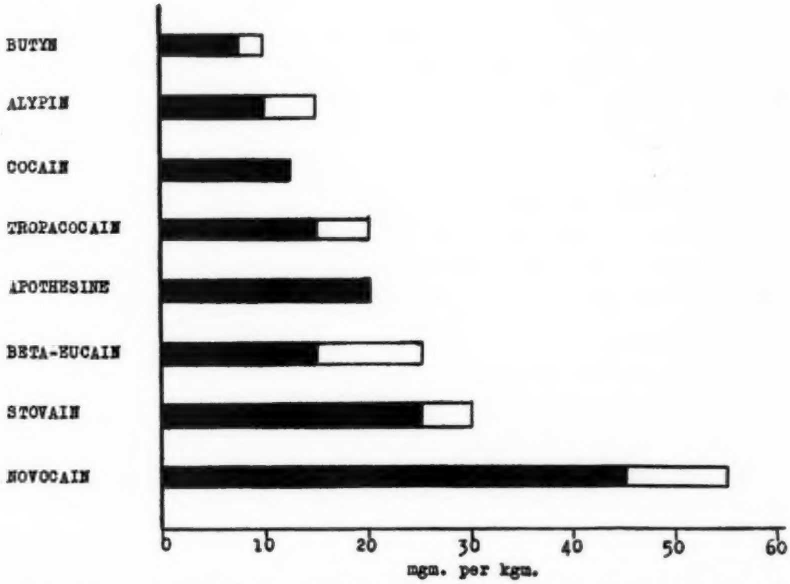

CHART I. A Quantitative Comparison of the Toxicity of the Alkamine Esters of Aromatic Acids Used as Local Anæsthetics. Rats Injected Intravenously. Maximal Tolerated and Minimal Lethal Dose in Milligrams per Kilo Body Weight.

died is considered the maximal tolerated dose. The dose at which the majority of a series died is considered the minimal lethal dose.

The abscissæ represent the number of milligrams of the drugs injected per kilo body weight. The shaded portions of the ordinates show the maximal tolerated doses, the unshaded portions the minimal lethal doses. The chart shows that butyn is the most toxic of the alkamine esters of the aromatic acids used as local anesthetics. The maximal tolerated dose is 7.5 milligrams and the minimal lethal dose 10 milligrams. The maximal tolerated dose of cocain as well

as the minimal lethal dose is 12.5 milligrams. The maximal tolerated dose of apothesine, as well as the minimal lethal dose, is 20 milligrams. The maximal tolerated dose of novocain is 45 milligrams and the minimal lethal dose is 55 milligrams.

In conclusion it may be stated without reservation that novocain is much less toxic than cocain or any of the alkamine esters of aromatic acids which have been introduced into practice.

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[From the Department of Experimental Medicine, H. A. Metz Laboratories.]

THE DRUGS OF THE NORTH AMERICAN INDIAN.*

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The drugs of our first landlords, the Aborigines of North America, represent an interesting group of products derived from the three great natural kingdoms. While the actual medicaments employed differ with the tribes and the regions in which they dwelt, many similarities are evident in their medical practices. Indian medicine of the past has been largely a mingling of charms and herbs. Where the Indians are in contact with the white man, many of the old remedies are slowly and stubbornly giving way to the newer curative agents of modern science.

To the uneducated Indians, the cause and nature of disease are for the greater part mysteries. Every illness that cannot be plainly associated with a visible cause is regarded as the effect of an introduction into the body of noxious objects either by a sorcerer or by offended or ill-disposed supernatural beings. These objects they believe produce the pain, discomfort and other symptoms of the illness.

Every Indian tribe had, and in many cases still has, its medicine men and medicine women who are distinguished in

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designation, responsibilities, and in influence over the people. The ordinary procedure of the medicine man was about as follows:

He first inquired into the symptoms, dreams, and transgressions of tabus of the patient, whom he examined, and then gave his opinion as to the nature of the ailment. This was generally mythical. He then prayed, advised or sang to the accompaniment of a rattle, and made passes with his hand, occasionally moistened with saliva, over the part affected. Finally, he placed his mouth over the most painful spot and sucked hard to extract the immediate principle of the illness. This result he apparently accomplished, often by means of sleight of hand, producing the offending cause in the shape of a pebble, thorn, hair, splinter, or other object, which was then thrown away or destroyed. Finally he administered a medicine and often with it, a protective fetish.

The fetishes used included peculiar shaped stones, feathers, claws, lightning-riven wood, hair, and pieces of pottery ornamented with mythic animals, representations of the sun, lighting, etc. These were believed to embody a mysterious power capable of preventing disease and counteracting its effects. There were numerous variations of this method according to the requirements of the case. If the case would not yield to simple treatment, a healing ceremony was sometimes resorted to. If all means failed, the medicine men suggested a witch or wizard as the cause. The designation of some known person as the culprit often placed his life in jeopardy. Often, when the medicine man lost several patients in succession, he was suspected by his tribe either of having been deprived of his supernatural power or having become a sorcerer, the penalty for which was usually death.

The medicine man was usually well compensated for his services. In early days, if an acceptable gift did not accompany the call for these, he demanded and received his fee in advance from the patient or family. Payment, then, was usually made in the shape of wampum, moccasins, the best bow, arrows, furs, venison or other food.

Of the many drugs constituting the Indian materia medica, by far the greater number are derived from the plant kingdom. The majority represent roots and rhizomes and entire plants, although barks, leaves, stems, flowers, fruits, pollen and seeds were also employed. These are used in the fresh or dry state. Usually only

a single drug is used for an ailment but among some tribes up to four drugs are combined in a single remedy. Relatively few animal and mineral drugs were used. The preparations which the Indians made from these drugs included decoctions, infusions, ointments, plasters, lotions and liniments. The greatest number were decoctions. Boiling was often done in dishes of birch or some other bark placed on coals, hot ashes, or stones heated by fire beneath, or heated stones were dropped into the liquid.

Before the arrival of the early colonists, the North American Indians were acquainted with cough and cold remedies, emetics, cathartics, diaphoretics, vermifuges, astringents, alteratives, stimulants, narcotics, and antiseptics. They did not know how these produced the desired effect; they simply knew they cured.

Some of their medicines were used because of a real or fancied resemblance to the part affected, others for traditional reasons, some because of a supposed supernatural beneficial effect, while others were left with the patient as protective fetishes. The ceremonies which accompanied the administration of many of the remedies varied with the tribes and healers. Some of these like the Mountain Chant which was practiced by the shamans or medicine men of the Navaho were occasions where people gathered together for a jolly good time at the patient's expense.

In return for the liberality, the patient hoped to incur the favor and help of the gods, the praise of the priesthood and social distinction from fellow tribesmen. This particular ceremony lasted nine days and was very costly. It included an elaborate program of dances and chants and little treatment.

Let us now examine a representative number of the drugs used by the North American Indians and the purposes for which they were employed.

Vegetable Drugs Used by the North American Indians.

1. *Balsam Fir.*—The Penobscot Indians of Maine prepared an ointment by incorporating the oleoresin of this tree with animal fat. The oleoresin is obtained from vesicles on the bark and also by skimming it from the surface of water in which the crushed bark is boiled. The oleoresin or balsam of fir was applied externally by various northern tribes to cuts and sores. The Ojibwa tribe of Minnesota used it internally as a remedy for gonorrhea and for

colds in the chest. They also scraped the bark from the trunk and prepared a decoction of it for inducing perspiration.

2. *Milfoil.*—The Winnebago employed an infusion of this herb to bathe swellings. A wad of leaves as well as some infusion was placed in the ear for earache. The Pah Utes make a tea from the plant which they drink for weak and disordered stomach.

3. *Sweet Flag.*—In early days the Indians mixed the powdered rhizome and roots with powdered red willow bark and used the mixture for smoking. All of the Indians employed the rhizomes as a carminative. The Plains tribes drunk a decoction for fever and colds and chewed it as a remedy for cough and toothache. They often employed it in the smoke treatment for colds. Among the Teton-Dakota, warriors chewed the rhizome to a paste which they rubbed on their faces to prevent excitement and fear when confronted with an enemy. The Cheyenne tribe believed the rhizome when chewed and rubbed on the skin to be good for any malady. They tied portions of the rhizome to the dress, blanket or necklet of their children to keep away the night spirits. The leaves were worn by various tribes as garlands.

4. *Maidenhair Fern.*—A decoction of this plant was used by the Cherokee in the treatment of chills and fever. A poultice prepared from this and usually some other fern was administered for rheumatism along with the decoction. The medicine men of this tribe explain that the fern is rolled up in the young plant but unrolls and straightens out as it grows and consequently a decoction of ferns causes the contracted muscles of the rheumatic patient to unbend and straighten out in like manner.

5. *Peyote.*—The drug obtained from this cactus is commonly known under the names of "peyote," "pellote" and "mescal button." It consists of the dried flowering top or crown of a succulent, spineless cactus, having the shape of a carrot, with a depressed globular head and a tapering tap root. This drug was used by the ancient Aztecs of Mexico who termed it "teonanacatl" or "sacred mushroom," on account of the resemblance of the dried buttons to peltate fungi. They imparted their knowledge concerning its use to the Chickimecas who in turn gave instructions to our Apaches, Co-

manches and Kiowas. It occurs in commerce as dried brownish disks, representing transverse slices of the crown, from 1 to 1.5 inches in diameter and about one-quarter inch in thickness; when dry it is hard and brittle but upon moistening becomes soft; its odor is peculiar and disagreeable and its taste unpleasantly bitter. From time immemorial this narcotic has been used in ceremonies of worship among the Mexican Indians. From these the Peyote religion has spread northward until now it has become a popular cult posing as a Christian religion among many of the Plains Indians. Its followers have become so strong in Oklahoma as to establish there a Peyote Church which is chartered under the name of the Native American Church.

The ceremony connected with a Peyote meeting is usually that of prayer, performed as an invocation for the recovery of some sick individual. It is held in an enclosure called a tipi and usually begins at night and continues until sometime the following morning. As many men as can sit comfortably within this "sanctum" participate while the women prepare the sacred food. In the center of the tipi a fire is kept burning, inclosed within a crescent-shaped mound on the top of which rests a sacred peyote. The opening prayer is delivered by the chief priest, after which four peyotes are distributed to each participant, who chews and swallows them. The sacred songs now begin to the accompaniment of the drum and rattle, each man in turn singing four songs. These continue all night, there being interims of payer and further distributions of peyote, with a peculiar baptismal ceremony at midnight. From ten to forty peyote disks are eaten by each individual. The drug is said to first usually produce a peculiar excitement of the brain, expressing itself in a feeling of contentment and a friendly attitude toward the world in general. This feeling is soon followed by a derangement of the centers of sight in the brain, which causes, particularly when the eyes are closed, a kaleidoscopic flow of scenes of great beauty and color effect. The Indians interpret these pleasing visions as a reflection of the beauties of paradise. The effect is heightened by the weird songs, the constant sound of the drum and rattle and the glare of the fire. The meeting closes with a feast in which the women participate with the men.

Peyote is also taken in the form of decoction or tea as well as in capsules of the ground disks. An excessive dose of the drug has a tendency, often, to cause unpleasant scenes in which hideous monsters and beings of distorted shape appear. The Indians are said to

interpret these visual hallucinations as denizens from the abode of evil spirits sent as a warning to them to forsake their evil ways.

6. *Spikenard.*—Many of the tribes used the rhizome and roots as a carminative as well as an expectorant and antiseptic in coughs, pains in the chest and mortification. The rhizome and roots and horseradish roots were ground and made into a poultice which was applied to the feet in general dropsy. The juice of the berries and oil of the seeds were poured into the ears of those afflicted with deafness.

7. *Jack-in-the-pulpit.*—The corm was used by the Pawnee who powdered it and dusted the powder on the top of the head and temples for headache. The powdered corm was also applied as a counter-irritant for rheumatism and muscular pains.

8. *Virginia Snakeroot.*—The Cherokee Indians employed the rhizomes and roots for a number of purposes. The drug was chewed and spit upon the wound to cure snake bites. It was bruised and placed in a hollow tooth for toothache and held against a nose made sore by constant blowing, in colds. A decoction was blown upon the patient for fever and drunk for cough.

9. *Canada Snakeroot.*—The Indians of Canada and Maine employed the rhizome and roots as a remedy for stomach ills.

10. *Pleurisy Root.*—The Penobscot Indians employed the root as a diaphoretic and cold medicine. The root was eaten raw by other tribes for pulmonary troubles. It was also chewed and put into wounds or pulverized, when dry, and blown into wounds and also applied as a remedy to old obstinate sores. In the Omaha tribe a certain member of the Shell society was the authorized keeper of this medicine. It was his duty to dig the root and distribute bundles of it to the members of the society. The ceremonials connected with the digging, preparation, consecration and distribution occupied four days. The No. 4 is dominant in all ritual and in all orientation in space and time among the Plains tribes, just as the No. 7 is dominant with other Indian tribes; whether four or seven be the dominant number depends on whether the four cardinal points of the horizon are given pre-eminence or whether equal place is given also to the three remaining points, the Zenith, the Nadir and the Here.

11. *Rattlesnake Fern.*—The Ojibwa bruised the root of this fern and applied it to cuts.

12. *Sweet-scented Water-Lily.*—The astringent rhizomes were greatly esteemed by Indian squaws who prepared a decoction from them for use as an internal remedy and injection or wash for leucorrhœa. The Penobscot and other tribes living in territory bordering the Atlantic seaboard used them as an application in the form of poultice to suppurating glands.

13. *Blue Cohosh.*—The rhizomes and roots were used for a number of ills by many tribes of Indians. They were esteemed their most valuable parturient. An infusion of this drug given a week or two before confinement is said to have rendered delivery rapid and painless. The drug was also employed as a remedy for rheumatism, dropsy, uterine inflammation and colic. The Omaha tribe considered a decoction of this drug as their greatest febrifuge.

14. *Pipsissewa.*—This plant was used by the Aborigines as an application to open sores and also internally as a tonic and diuretic.

15. *Water Hemlock.*—The roots of this poisonous herb were eaten by such Indians as were tired of life and desirous of an early demise.

16. *Black Snakeroot.*—This was a favorite remedy among the Aborigines of the eastern half of North America. The rhizomes and roots were used by them for rheumatism, disordered menstruation and slow parturition. They were also used against bites of poisonous snakes.

17. *Kinnikinnick.*—The inner bark of this dogwood was scraped off and dried for smoking by most of the tribes. The tobacco mixture of the North American Indians called "Kinnikinnick" is composed of scrapings of the bark of this species mixed with tobacco in the proportion of about one in four. The Cree Indians of Hudson Bay used the bark in decoction as an emetic in cough and fever. They made a black dye by boiling it with iron rust. A scarlet dye was made by several tribes by boiling the rootlets with water.

18. *Flowering Dogwood.*—At the time of the discovery of America, the Delawares and other tribes used the bark for fever and colds.

19. *Showy Lady's Slipper.*—The Penobscot tribe employed the rhizomes and roots of this orchid as a sedative in nervous disorders.

20. *Smaller Yellow Lady's Slipper.*—The Cherokee employed a decoction of the rhizomes and roots for worms in children. In this liquid was placed some stalks of a chickweed. From the appearance of the red fleshy stalks of the latter, it was supposed to have some connection with worms.

21. *Jimson Weed.*—The Indians of Southern United States and Mexico knew the narcotic properties of this annual herb before the arrival of the white man. The Virginia Indians gave it as an intoxicant in initiatory ceremonies. The Walapac of Arizona used the decoction of leaves, roots and flowers to induce frenzy and exhilaration. The Zuni of New Mexico use the roots as a narcotic and anæsthetic and employ the powdered blossoms and roots externally in the treatment of wounds and bruises. They formerly used Datura seeds to divine the hiding place of some precious object or to detect the thief who had stolen it. Some of the Yuman tribes employed the leaves only as a narcotic. Among the Aztecs of Mexico the seeds of a Datura were held sacred and the spirit of the plant was invoked to expel evil spirits.

22. *Canada Fleabane.*—The Cree Indians used a decoction of this composite for diarrhœa. The Zuni used the ray florets only. These they crushed between the fingers and inserted in the nostrils to cure rhinitis.

23. *Button Snakeroot.*—This plant was popular with many tribes as a remedy for snake bites. It was combined with Blue Flag as a febrifuge and diuretic.

24. *Wahoo.*—A decoction of the inner bark was drunk by the Winnebago squaws for uterine trouble.

25. *Boneset.*—A decoction of this plant was regarded by the native tribes as one of the most powerful remedies for fever and colds.

26. *Joe Pye Weed.*—The Cherokee employed a decoction of the root for difficult urination.

27. *Jalap.*—The Mexican Indians used the tuberous root of this plant as a drastic purgative.

28. *Cranesbill.*—The rhizome was used by several of the eastern tribes as an astringent in diarrhœa. The Cherokee employed a decoction of this drug and Chicken Grape for washing the mouths of their children in thrush.

29. *Bowman's Root.*—The emetic virtues of the root of this herb were known to many of the Indians who made the early colonists acquainted with its properties. The Cherokee tribe also used the root which they pounded up and applied as a poultice to swellings.

30. *Grindelia.*—A decoction made from the entire plant was drunk by the Indians of Mexico and Southern California as a cure for colds. The Ponca tribe used a decoction for consumption, while the Teton-Dakota administered it to their children as a remedy for colic. The Pawnee boiled the tops and leaves and made a wash for saddle galls and sores on horse's back.

31. *Witch Hazel.*—Many of the tribes used an infusion of the bark for bruises, piles and hemorrhages.

32. *Hepatica.*—The Cherokee made a tea from this herb or chewed the root for coughs. Those of this tribe who dreamt of snakes took a decoction of this plant and the Walking Fern. This produced vomiting and it was believed the dreams did not return.

33. *Cow Parsnip.*—The tops are used by the Winnebago medicine men in the smoke treatment for fainting and convulsions. A decoction of the root is employed by the Omaha tribe as a remedy for intestinal pains and as a physic. The Pawnee scrape or powder the root and after boiling apply the mass to boils as a poultice.

34. *Hop.*—The fruits were made into a tea by the Teton-Dakota which was used for fever and abdominal pains. This and other Plains tribes chewed the root and applied it to wounds, sometimes in combination with the roots of a Ground Cherry and Meadow Anemone.

35. *Yellow Puccoon.*—This valuable plant was known to the Cherokee before the arrival of the early settlers. This tribe had used its rhizomes and roots with success as a tonic, stomachic and as an application to sore eyes and ulcers. A yellow dye for clothing and implements of warfare was also prepared by them from this drug.

36. *Waterleaf.*—The roots were boiled by the Ojibwa who took the liquid for internal pains, especially those occurring in the back or chest.

37. *Cassine.*—This shrub also called Yaupon, was the source of the celebrated ceremonial "black drink" of the Aborigines. The Creek Indians of Florida discovered it and imparted their knowledge of its valuable stimulating properties to the white settlers of Florida, Georgia and the Carolinas. The American Indians prepared the leaves for keeping by drying or rather parching them in a pottage pot over a slow fire. They drank large quantities without sugar for health and pleasure. They claimed it restored lost appetite, strengthened the stomach and gave them agility and courage in war.

René de Laudonnière, leader of the ill-fated Huguenot expedition to Florida (1564) observed the use of the "black drink" as practiced by the Indians living at the mouth of the St. John's River, Florida. Later, Le Moine, in his narrative of this expedition, gave the following account of the ceremonies accompanying the preparation and dispensing of the "black drink":

"The chief and his nobles are accustomed during certain days of the year to meet early every morning for this express purpose in a public place, in which a long bench is constructed, having at the middle of it a projecting part laid with nine round trunks of trees for the chief's seat. On this he sits by himself for distinction sake; and the rest come to salute him, one at a time, the oldest first, by lifting both hands twice to the height of the head and saying, 'Ha, he, ya, ha, ha.' To this the rest answer, 'Ha ha.' Each as he completes his salutation takes his seat on the bench. If any question of importance is to be discussed, the chief calls upon his lauas (that is, his priests) and upon the elders, one at a time, to deliver their opinions. They decide upon nothing until

they have held a number of councils over it, and they deliberate very sagely before deciding. Meanwhile the chief orders the women to boil some cassine, which is drunk prepared from the leaves of a certain root and which they afterwards pass through a strainer. The chief and his councilors being now seated in their places, one stands before him, and spreading forth his hands wide open, asks a blessing upon the chief and the others who are to drink. Then the cupbearer brings the hot drink in a capacious shell, first to the chief, and then, as the chief directs, to the rest in their order in the same shell. They esteem this drink so highly that no on is allowed to drink it in council unless he has proved himself a brave warrior.

"Those whose stomachs reject the drink are not intrusted with any difficult commission or military responsibility being considered unfit, for they often have to go three or four days without food; but one who can drink this liquor can go twenty-four hours afterward without eating or drinking. In military expeditions also the only supplies which they carry consist of gourd bottles or wooden vessels full of this drink. It strengthens and nourishes the body."

38. *Blue Flag.*—By most of the Indian tribes the rhizome of this perennial herb was highly esteemed as a remedy for gastric disturbances. The Omaha and Ponca tribes powdered it, mixed it with water or saliva and dropped this preparation in the ear for earache. They also prepared a paste from it which they applied to sores and bruises.

39. *Red Cedar.*—The leaves were used by the Cree Indians as a diuretic. The Ojibwa employed the bruised leaves and fruits as a headache remedy while the Plains tribes boiled together the fruits and leaves and drank the decoction for cough. For colds in the head and nervousness the twigs were burned and the smoke inhaled. The Oglala tribe used a decoction of the leaves internally in Asiatic cholera. The Omaha and Ponca heated the twigs on hot stoves in their purificatory rites.

40. *Indian Tobacco.*—The dried leaves of this Lobelia were smoked by many tribes as an emetic.

41. *Canada Moonseed.*—The rhizomes and roots of this climber was used by various tribes for scrofula. The Pawnee employed it for sore mouth.

42. *Indian Pipe.*—The juice of this plant is mixed with water and applied to sore eyes by several tribes who esteem it as a soothing and often curative medicine.

43. *Tobacco.*—The leaves of various indigenous species of *Nicotiana* were used as a drug before the discovery of America. Columbus, on landing at St. Domingo in 1492, discovered the natives smoking cylinders of tobacco leaves. The drug was so extensively used by the Indians that the early settlers found it under cultivation as far north as the St. Lawrence River.

The "Tobacco Nation," inhabiting nine villages just below the southern shores of Lake Huron, cultivated tobacco on a large scale and sold it to other tribes who used it in smoking. At meetings of ambassadors, treaties of peace and councils of nations, the calumet or pipe of peace was circulated. In the south, tobacco smoking often accompanied the ceremonial of the "black drink."

While smoking is the most common way of employing this drug, it is by no means the only method. The Tewa tribe place tobacco leaves on or in a tooth to relieve toothache and use tobacco snuff to cure a discharge from the nose. To cure a cough, they place tobacco, oil and soot in the hollows of the patient's neck and make a cross of tobacco on the chest.

44. *Prickly Pear.*—The pith of this plant was thrown on live coals by the Apache and the smoke allowed to pass into the open eyes.

45. *Ginseng.*—Ginseng was known to a number of tribes, the root being alone used. The Cherokee chewed the root and ejected it on the painful area. They drank a decoction of this drug for headache, cramps and female troubles. The roots were employed by several western tribes in combination with parts of other plants and red paint as a love charm.

46. *Poke Berry.*—The American Aborigines handed down the medicinal uses of this plant to the white settlers. They employed

the root as an emetic and rheumatism remedy and the fruit for a red stain which they used in decorative work.

47. *May Apple.*—The Aborigines used the rhizome and roots as a cathartic.

48. *Seneca Snakeroot.*—The Seneca tribe was the first to make the white man acquainted with the virtues of this plant. They employed the root in decoction as a remedy for coughs and colds as well as for the bite of a rattlesnake. They also used the leaves which were made into an infusion and given for sore throat.

49. *Solomon's Seal.*—The Cherokee bruised the root, then heated it and applied it as a poultice to remove swelling.

50. *Wild Black Cherry.*—The inner bark of this tree was applied to external sores. It was prepared for use either by first boiling, bruising or chewing it. An infusion of the inner bark was given by the Indians to relieve pain and soreness of the chest.

51. *White Oak.*—The root bark and inner bark of the trunk of this and other oaks was used by many of the tribes in the form of decoction for diarrhœa.

52. *Castor Oil Bean.*—The Maricoba tribe crushed the seeds, mixed them with water and heated the mixture. One or two drops of this was placed in the ear for earache.

53. *Early White Rose.*—The roots of this or other species of wild roses were steeped in warm water by most of the tribes and the liquid applied to inflamed eyes.

54. *Rumex.*—The root and green leaves of the Yellow Dock were used by many tribes as a medicine and dye. The Cheyenne drank an infusion of the powdered root for hemorrhage of the lungs. They also moistened the powdered root and applied it as a poultice to wounds and sores. The Ojibwa applied the bruised or crushed root to sores and abrasions. The Teton-Dakota crushed the green leaves and bound them on boils to draw out the suppuration.

55. *Sanguinaria.*—The rhizomes and roots of this plant constituted the "Red Puccoon" of the Indians generally who used it both as a red dye for painting their faces, clothing and implements of warfare and as a love charm. The fresh rhizomes and roots, containing a red milk juice were used for decorating their skin, while wearing apparel was often boiled with these parts. Bachelors of some of the tribes, after rubbing some of the red milk juice on their hands, would contrive to shake hands with girls they desired; if successful in this, after five or six days, these girls are said to have been found willing to marry them.

56. *Mad-dog Scullcap.*—This herb was long used by the Penobscot, Iroquois, Cherokee and other tribes, in decoction, as a remedy for numerous ailments. It is listed as an ingredient in one of the sacred formulas of the Cherokee. A decoction of this plant together with *Scutellaria pilosa, Hypericum punctatum* and *Stylosanthes elatior* was drunk by the women of this tribe to promote menstruation. It was also used by the men of the tribe as a wash to counteract the ill effect of eating food prepared by a woman in the menstrual condition. It was also drunk for diarrhœa and used with other herbs for breast pains.

57. *Indian Pink.*—The rhizomes and roots of this plant were valued as a vermifuge among the Aborigines before the discovery of America. The colonists of the South received their information concerning its properties from the Cherokee and Osages who also used it as a sudorific and sedative.

58. *Dandelion.*—The Tewa ground the dried leaves of this herb and used the powder in dressing fractures. They also mixed this drug with dough and applied it to bruises.

59. *Bethroot.*—The rhizomes and roots of this plant were used for women's complaints by the Indians of Missouri and Canada. The freshly cut rhizomes were held to the nose and the acridity inhaled for nose bleed.

60. *Hemlock.*—The Penobscot tribe used finely powdered hemlock bark to relieve and prevent chafing.

61. *Cat Tail.*—Every part of this plant was used by various Indian tribes for some ailment. The Cherokees crushed the roots by pounding or chewing and applied the mass as a poultice to sores. The Omaha tribe used the roots and ripe blossoms for scalds. For this purpose the root was powdered, wetted and spread as a paste over the scald. The ripe blossoms were then applied as a covering and the injured part bound, so as to hold the dressing in place. The Cheyenne used an infusion of the powdered roots and white bases of leaves for the relief of abdominal cramps. The Dakota, Omaha-Ponca, Winnebago and Pawnee applied the down as a dressing to burns and scalds. They also rubbed it on the skin of infants to prevent chafing. Newly born babies were laid in a mass of the down.

62. *Slippery Elm.*—The fresh inner bark was chewed for cough by many of the tribes. It was boiled by the Omaha who used the decoction as a laxative. This tribe as well as the tribes of Canada have long cooked the inner bark with all of their animal fats in rendering out the grease. These tribes have realized that the bark gives a desirable flavor to the fat and a preservative quality, preventing the rendered grease from becoming rancid.

63. *American Hellebore.*—The Indians of New England used the rhizome and roots as an ordeal in the selection of their tribal chiefs. The one whose stomach withstood its action the longest was decided to be the strongest of the party and entitled to command the rest.

64. *Culver's Root.*—The Ojibwa used a decoction of the rhizome and roots as a purgative.

65. *Cascara Sagrada.*—Some of the Indian tribes of the northwest employed this bark in decoction as a purgative.

66. *Sarsaparilla.*—The Mexican Indians employed the roots of the Mexican species in decoction as an alterative.

67. *Rhatany.*—The Indians of southern Texas and northern Mexico extensively employed the roots of a *Krameria* as an astringent.

68. *Aconite.*—The Otomi tribe pasted the leaves of an unidentified species of Aconite over the painful area, in treating neuralgia, and on the temples for headache.

69. *Red Baneberry.*—The Ojibwa, Sagamore, Penobscot and other tribes employed a decoction of the root for pains in the stomach. On account of its characteristics at certain seasons of the year, it was considered male and given only to men and boys; at other seasons, on account of the color of its fruits or some other peculiarity, it was considered female, and given only to women and girls.

70. *Aletris.*—The Aborigines living along the eastern seaboard used a decoction of the rhizome and roots of the Unicorn Root as a stomachic, tonic and emmenagogue.

71. *Pulsatilla.*—Bachelors of the Ponca tribe rubbed the tops of the native species into the palms of their hands as a love charm. The Pawnee gave the entire plant to horses as a stimulant. Other Indian tribes used the crushed leaves as a counter-irritant in rheumatism and neuralgia.

72. *Bearberry.*—The leaves were dried by several aboriginal tribes and ground with tobacco or red willow as a smoking mixture. A decoction of the stems, leaves and berries was drunk by many tribes for pain in the back and sprained back.

73. *Artemisia.*—Practically every native species of Artemisia was popular with the Indians of this continent. An Indian who had broken some taboo or who had touched any sacred object must bathe with Artemisia. It was always considered proper to begin any ceremonial by using Artemisia in order to drive away evil influence. Old timers used various Artemisias for exorcising evil powers. They employed sweet grass or cedar twigs as incense for attracting good powers.

There are Indians today who still use any of the Artemisias as incense for this purpose at Christmas, Easter, Pentecost and on the occasion of funerals.

Decoctions of various species of Artemisia are highly valued by the tribes for stomach troubles, colds, worms, and other ailments.

74. *Trailing Mahonia.*—The rhizome and roots of this Barberry has been a favorite drug of the California Indians. A decoction is taken as a remedy for general debility and as an appetizer.

75. *American Wormseed.*—The entire herb was employed by the Aborigines in a tea for painful menstruation.

Animal Drugs.

Rattlesnake.—Among the Cora tribe, a patient suffering from consumption hunted a rattlesnake and cut off its head and tail before it became angered. The body of the snake was then washed, toasted and dried and a piece of it taken at each meal. The Papago also used the flesh of the rattlesnake for the same disease but prepared it differently. They dried the flesh and powdered it and mixed a portion of this powder with the patient's food while it was being cooked and without his knowledge. The Pima applied the fat of this animal to wounds induced by the rattlesnake. The Hopi and other southwestern tribes treated such wounds with an application of the ventral surface of a disemboweled snake. A secret decoction of herbs was also given to the patient.

Beaver (Castor).—The Penobscot tribe used the preputial follicles of the beaver as a remedy for irregular menstruation.

Pig.—The Cora tribe employed the snout and blood of a recently killed pig in the treatment of snake bites. The raw surface of the snout was applied to the wound, and the blood, diluted with warm water, was drunk.

Cricket.—The insects were dried, and ground, and taken internally as a remedy for dysuria by the Papago.

Lizard.—This reptile was used by the Tarahumare and Cora tribes who employed it in the form of decoction for bodily pains.

Spider.—Spider's eggs were used by the Apache as medicine. The Mescaleros and other tribes applied the spider's web to cuts to stop bleeding.

Owl.—The Pima employed the feather of this bird for curing a person who steadily loses flesh and feels ill.

In addition to these, the oils and fats of buffalo, bear and other animals were used as liniments and as bases for ointments.

Mineral Drugs.

Red Ochre.—The Navaho and other tribes mixed this with fat and rubbed the ointment on the skin to prevent sunburn.

Slaked Lime.—The Cora applied slaked lime as a dressing to gunshot wounds.

Ashes.—The Hopi blow wood-ashes on an inflamed surface to counteract the supposed fire which causes the ailment.

Clay.—The White Mountain Apache women employed the red, barren clay from beneath a camp fire to induce sterility.

The Indians of North America had a more extended acquaintance with the materials of medicine than has generally been believed. While some of their practices were shamanistic and a number of their remedies worthless, they employed many drugs of real value. Among the drugs which they used the following are officially recognized either in the present editions of the United States Pharmacopœia or the National Formulary:

Seneca Snakeroot, Pleurisy Root, Poke Root, Yellow Dock, Jalap, Blue Flag, Beth Root, Geranium, American Hellebore, Black Snakeroot, Golden Seal, Bloodroot, Virginia Snakeroot, May Apple, Pink Root, Aletris, Lady's Slipper, Angelica, Canadian Hemp, Spikenard, Canada Snakeroot, Trailing Mahonia, Blue Cohosh, Purple Cone Flower, Culver's Root, Cascara Sagrada, Sarsaparilla, Wild Black Cherry, Slippery Elm, Prickly Ash, Sassafras, Dogwood, Wahoo, Butternut Bark, White Oak Bark, Rhatany, Blackberry Root Bark, Yerba Santa, Jimson Weed, Bearberry, Witch Hazel, Pipsissewa, Arbor Vitae, Grindelia, Lobelia, Boneset, Scullcap, Pulsatilla, Life-Root, Verbena, Elder Flowers, Hops, Vanilla, Pumpkin Seeds, Larch Agaric and Turpentine. A number of others have appeared in former editions of these works.

From the Red Man of this continent, our forefathers gained knowledge of many of the uses of these drugs which has been passed down to the present generation as a valuable heritage.

THE DETECTION OF DIETHYL PHTHALATE.

Henry Leffmann.

The introduction of diethyl phthalate as a denaturant for commercial alcohol has rendered important the methods of detecting it in small quantity in order to determine whether alcoholic beverages offered for sale or found in the possession of unauthorized persons have been prepared from such denatured material and thus escaped taxation. It is assumed by the authorities that the bitterness of the ester will prevent the beverage use of the liquor containing it, but this is doubtful in view what is now known concerning the risks that habitual drinkers will run. Notwithstanding this doubt, the denaturing of strong alcohols by about 2 per cent. by volume of the ester has been permitted by several of the leading nations, including the United States. Whether the compound is distinctly poisonous or merely disagreeable seems not to be definitely settled. It has been stated by Dr. E. Payr, Director of the University surgical clinic at Leipzig, that alcohol containing diethyl phthalate is locally irritating, causing much scurf skin, some eczema and anesthesia of the finger-tips.

A review of the facts in regard to the ester, especially of the methods for its detection is presented by F. Utz, in a recent issue of the *Pharmazeutische Zentralhalle* (1924, *65*, 201). He reviews the tests heretofore suggested for its detection which depend, of course, on the property of phthalic compounds to yield complex derivatives of distinct and characteristic colors. The authorized German process depends on the use of pyrogallol. Utz has not found this satisfactory, and a substitution of diphenylamin did not give appreciably better results. In "Schimmels' Report" (1923, 137) the method of Lyons is described. This depends on the reaction between the phthalic compound and resorcinol producing the vividly fluorescent resorcinolphthalein. Calvert (Amer. Jour. Pharm., 1922, *94*, 702) substituted phenol for resorcinol, thus obtaining the characteristic phenolphthalein. Calvert's method has the advantage that the color of phenolphthalein is clear and unmistakeable, while in some cases a slightly turbid liquid may be mistaken for a fluorescent one. Andrews (*J. I. E. C.*, 1923, *15*, 838), described an improved method with resorcinol, saponifying the ester with sodium hydroxide solution.

These tests are directly applicable to alcohols containing no appreciable amounts of extractives or medicinal substances, but in case such substances are present separation of the ester by means of light petroleum is necessary. This solution is evaporated spontaneously and the residue re-dissolved in alcohol.

Failure on the part of Utz to get entirely satisfactory results led him to seek better methods, and he finally determined upon a modification of Lyons' method as follows:

For spirits containing no appreciable amount of other substances than the alcohol and ester, 1 cc. of the sample is placed in a test-tube (best of a resistance glass) and 1 cc. of strong sulphuric acid added. The mixture is heated over a small flame until the alcohol is driven off and white fumes of the acid appear. The liquid will have acquired a reddish tint if the ester is present. The mixture is allowed to cool somewhat, a pinch of resorcinol added and again heated until it becomes brownish red, and when allowed to spread on the sides of the tube appears somewhat like strong solution of ferric chloride. The mass must be then cooled to room temperature and excess of ammonium hydroxide added. Obviously this addition must be made cautiously. The solution acquires a distinct fluorescence at the upper edge, when the alkalinity is attained, but the vividness is greatly increased by pouring the mass into about 500 cc. of water. Distilled water is not required.

A trial of this method showed very satisfactory results. A minute amount of the ester gave an intensely fluorescent solution. It seems to be simpler and quicker than the methods heretofore suggested. Alcoholic liquids containing appreciable quantities of other substances than the ester, alcohol and water must be extracted with light petroleum as directed in the other processes. The method avoids the saponification of the ester by sodium hydroxide and the subsequent fusion. The addition of strong ammonium hydroxide to strong sulphuric acid is attended by some inconvenience, and it occurred to me that this can be avoided by pouring the acid liquid into a rather large volume of water strongly alkalized by sodium hydroxide. Experiment showed this to be the case. I have also found that a satisfactory test can be obtained by mixing the 1 cc. of strong sulphuric with 1 cc. of the liquid to be tested and placing the mixture in an evaporating dish, which is then heated on the water-bath until the volume is much reduced. The mixture is

transferred to a test-tube and heated as directed. After the second heating—after addition of resorcinol—the liquid is allowed to cool and a small amount of it poured into the water to which sodium hydroxide has been added as noted above. Very small amounts of diethyl phthalate gave highly vivid flourescence. I have found that good results can be obtained when considerable amounts of commercial methanol are present. Isopropyl alcohol does not seriously interfere, but when in large proportion seems to diminish the fluorescence by the presence of a turbidity. Commercial methanol blackens very much when heated with sulphuric acid, and commercial isopropyl alcohol produces some darkening.

Notwithstanding the practical advantages of Utz's method and the great delicacy of it, experiment showed that misleading results may be obtained. Blanks gave fluorescent liquids, which though faint, and lacking the vividness of the true fluorescein, were yet quite sufficient to lead to the view that the phthalate was present, although none had been added. A comparison of the several procedures showed the Andrews' is especially simple and dependable.

Tests were made to determine how far the substances likely to be present in recovered or imperfectly prepared alcohol might interfere with the accuracy of Andrews' method. One cc. of phthalate was dissolved in strong alcohol and made up to 100 cc., of which 1 cc. was diluted to 100 cc. with alcohol. Twenty cc. of this was mixed with small amounts of acetaldehyde, commercial methanol and commercial isopropyl alcohol. A control liquid of similar composition without the phthalate was prepared and 20 cc. also tested. The results were very satisfactory. Mr. Foran, though unaware of the identity of the two results, picked out the tube containing the liquid derived from phthalate at once, as this showed a distinct fluorescence, while the other liquid had no such appearance.

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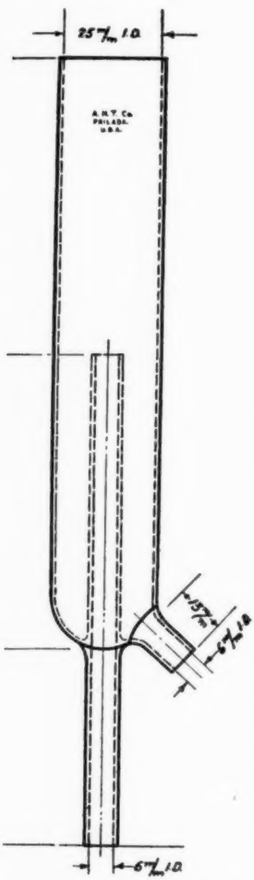
A MICRO-DISTILLATION APPARATUS.

By Henry Leffmann.

The enforcement of the prohibition laws has brought about the sale of considerable intoxicating liquor obtained either by irregular manufacture or recovered from denatured forms. Chemists have been much occupied of late in devising and applying tests for the impurities that may be present in illicit samples. In most cases it is necessary to resort to distillation of a portion of the sample, and LaWall has shown (This JOURNAL, 1924, *96*, *226*), that in view of the possible presence of small amounts of glycerol, distillation is absolutely necessary when testing for methanol by U. S. P. method as modified by him. As the quantity of distillate required is small, it is inconvenient to use the ordinary apparatus with water-cooled condenser, and having occasion to make a number of tests in which distillation on a small scale was required, I had constructed the apparatus shown in the annexed cut. The drawing is half the size of the original. The tube is fastened in a convenient clamp, and a tube about 50 cm. long with a bore of about 1 cm., is passed through a cork that fits snugly in the upper opening of the special tube. It is best to cut the lower end of long tube diagonally in order to facilitate the dropping off of any liquid, and it is also advisable to bore the cork eccentrically so that the opening of the tube may be well to one side of the special tube, that condensed liquid will not drop back into the distilling flask. The narrow tube that goes through the bottom of the special tube is, of course, fixed by means of a perforated cork, in a conical flask of convenient size. The exit tube permits of drawing off the distillate as desired. As



MICRO-DISTILLATION APPARATUS.

the cork that is used for closing the exit tube may absorb minute portions of the distillate, it will be safer to have a supply of that size and use a new cork for each operation. Another arrangement, however, can be made, that is, to close the exit by the attachment used on non-stoppered burettes, a piece of rubber tube plugged with a piece of glass rod. A small tube drawn out to form a jet will serve as a convenient delivery. By this arrangement portions of the distillate can be drawn off at will. The apparatus will thus serve for approximate fractionations. It is an advantage to indicate on the tube that receives the distillate the approximate point at which the accumulated liquid amounts to, say, 20 cc., which is a convenient amount for test. Distillation is rendered more satisfactory if a piece of water-logged pumice is placed in the flask. This is prepared by heating small fragments of pumice to redness and dropping them at once into cold water. Most of them will sink promptly and remain so. Distillation should be conducted somewhat slowly, and there will be no appreciable loss by the upright condensing tube. As the receiving tube becomes somewhat hot, the liquid should not be drawn off until some time has elapsed after the distillation has been stopped.

I have used the apparatus a number of times and found it very satisfactory. All the glass parts are easily cleaned when they are cold.

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STUDIES OF TESTS FOR ACETONE AND ALDEHYDES.

By Henry Leffmann.

About twenty years ago, Viktor Frommer published in the *Berl. klin. Wochensch.* (1905, *42*, 1008), a test for acetone, especially intended for detection in urine. It depends on a reaction with salicyl aldehyde in strong alkaline solution. The procedure is to add 1 gram of solid potassium hydroxide to 10 cc. of the sample, then a dilute solution of the aldehyde in strong alcohol and warm to 70°. The reaction is prompt and distinct, but the aldehyde is not a familiar reagent of the laboratory; it occurred to me to experiment with some more familiar substances, and I have found that vanillin gives a satisfactory reaction. The test may be performed by adding to

about 10 cc. of the sample, a few cc. of a 10 per cent. solution of vanillin in dilute alcohol, and dropping in a small fragment of solid sodium hydroxide. Direct heating of the liquid is not necessary, as the heat of solution of the hydroxide is sufficient. A strongly marked red ring forms above the alkaline solution. Trial of the method by comparison of a sample of urine recognized by the customary clinical tests as containing acetone with a sample of normal urine indicated that clear distinction can be made. After standing about a half hour the sample containing acetone had produced a well-marked red ring, while no such appearance was observed in the normal sample. Standing overnight the acetone sample showed a diffused redness, but the other had no trace of such color.

Nessler's solution reacts with acetone to produce a precipitate that is a combination of mercurous iodide with the ketone. Attention seems to have been first called to this fact in 1889 by C. Gillet, but the matter was overlooked, and in 1908, Marsh and Struthers communicated to a meeting of the Chemical Society (*J. C. S.*, Proc., 1908, *24*, 266), some experiments on the action of alkaline mercuric solutions on acetone. Recently Gillet made a communication to the French Chemical Sceiety (*Bull. Soc. Chim.* [4], 1923, *33-4*, 465), giving further details of the reaction, but it seems to be suitable only to fairly pure solutions. In many cases, distillation would give a suitable solution, but Frommer states in connection with his test give above, that in distilling urine, any acetoacetic acid that may be present will be converted into acetone and thus mislead.

E. Pittarelli has made an extensive investigation into the reactions of formaldehyde, acetaldehyde and acetone. His results have been published in *Archivio di Farmacologia Sperimentale e Scienze Affine*. The principal data are in the issue 1920, *29*, 81. Among the most interesting are the reactions of these substances with hydroxylamine hydrochlorine and hydrazin sulphate.

Abstracts of this article have appeared in several publications, including the Year Book of the American Pharmaceutical Association (1921, *10*, 400). I have also consulted the original article. Pittarelli states that acetaldehyde decomposes hydrazin sulphate in definite proportion, liberating an equivalent of sulphuric acid for each molecule of the aldehyde, while acetone is without action. With hydroxylamin salts, both substances react, liberating the equivalent of acid. Experiment showed that the reactions of acetone and

acetaldehyde with the hydrazin salt are quite different, but with hydroxylamin hydrochloride the reaction seems to be delayed, so that after titrating to alkalinity, the liquid in a few minutes passed again to an acid condition. Further experiment will be needed to determine the exact conditions of accuracy.

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ABSTRACTED AND REPRINTED ARTICLES

HYDROGEN-ION CONCENTRATION IN RELATION TO ANIMAL AND PLANT GROWTH.*†

By Henry Leffmann, A. M., M. D.

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Sourness is so characteristic a taste, that it must have been recognized as a specific property of some common substances at a very early period of human history. In modern science it is especially noted as a characteristic property of a class of bodies termed "acids." No instance of distinct sourness unassociated with some degree of acidity seems to be known, but compounds are known which have the main characteristics of acid, yet are not appreciably sour. Sourness is not the only noticeable property of acids. Power to dissolve substances insoluble in ordinary liquids is also a striking feature of many. In ancient times but one acid seems to have been recognized as a specific substance, namely, acetic. This exists in moderate proportion in vinegar, and is the result of the exposure of dilute alcoholic liquids to air, by which certain forms of minute organisms are introduced and the alcohol is oxidized to a limited extent. As the part played by these minute organisms has only been recognized within recent years, the change of alcohol to acetic acid was long regarded as "spontaneous" and was so termed. The same erroneous view was held regarding

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†Reprinted from *Journ. of the Franklin Institute.*

the fermentation of amylaceous and saccharine substances into alcohol, and the putrefaction of organic matters generally.

A review of the early history of acidity and of the discovery of the important types of acids is to be found in the great chemical classic, Hermann Kopp's "Geschichte der Chemie," in the third volume, under the title "Entwicklung der Kenntnisse über die Säure" (Development of knowledge concerning acids). Acetic acid was designated in both Greek and Latin by words akin to those indicating sourness—Greek, *oxos,* vinegar, *oxus,* sour; Latin, *acetum,* vinegar, *acidus,* sour. *Dioscorides* (first century) gives no specific information, but Pliny the elder states that vinegar produces foaming with certain earths. Of course, natural carbonates are meant. Vinegar derived from both wine and cider was known to the Jews, and a sentence in Proverbs (25:20) refers to the foaming produced by one of these forms. Kopp gives Luther's translation of the Hebrew text—"Essig auf der Kreide"—vinegar on chalk, but the modern critics read "soda," sodium carbonate being intended. The Hebrew word has the consonants "NTR," which probably was the cause of the King James Bible reading "nitre." The knowledge of the solvent action of vinegar on some familiar substances led to extravagant claims for its power. Ancient writers, including Livy and Plutarch, state that Hannibal in his journey over the Alps used vinegar to dissolve the rocks, and Vitruvius claims that it can dissolve rocks that are not affected by fire or iron.

Recognition of the power of vinegar to cause not only foaming, but to form new compounds was a step forward in the differentiation of the group, a conception that was extended when other acids were discovered. It is not necessary to set forth here in detail what might be termed the "lore of acidity," but a few salient points will not be inopportune. Kopp credits Geber with the first reference to nitric acid, called "parting acid," because used in the parting of gold and silver—dissolving the silver out from alloys of the two metals—but Berthelot has thrown considerable doubt on the genuineness of some of the works ascribed to Geber, so that the reference must be used with caution. The term "parting acid," however, persisted until a comparatively recent period as a trade name for a certain strength. The Greek alchemists of the early centuries of the present era added considerably to the list

of acids and to a knowledge of their properties. In a much later period Basil Valentine (fifteenth century) discovered hydrochloric acid and improved the method of making sulphuric acid. Naturally, the possession of these three powerful acids must have aided greatly in the development of chemistry. Organic acids, as a group, were recognized about the beginning of the seventeenth century, when Mayerne discovered benzoic acid and Croll succinic. About a century later, Hiärne's observations on formic acid, attracted notice as an acid of animal origin. Scheele showed the existence of acids derived from metals, and Boyle pointed out the action on certain vegetable colors with the contrary action of alkaline substances. In 1723, Fr. Hoffmann classified the gas escaping from some spring waters as an acid, because of its action on litmus. This was carbonic acid.

In the latter half of the eighteenth century, when the civilized world was wrestling with great wars, and especially with the revolt of the American colonies, chemists were investigating the relation of acids to the substances that were capable of saturating them, and a large amount of quantitative data was obtained. The identification of oxygen was an important step forward, and in the laboratory of Lavoisier its relation to acidity was considerably developed. In 1781, Lavoisier presented a memoir to the Paris Academy in which he stated that in the future he would term the gas that he had found to produce acids with some substances and bases with others, "oxygen" (producer of acid), and since that time the word has come into most languages with only slightly modified forms. German, however, in accordance with its system has translated the word into its own roots and calls it "Sauerstoff."

Lavoisier burned sulphur and carbonaceous materials in oxygen and obtained solutions which reddened vegetable colors and neutralized metallic oxides. He assumed, therefore, that the acidity thus produced was due to the gas that he was using and hence the name he gave it. He overlooked the fact that water was present in all these experiments, and we now know what an important part it plays in determining acidity. The discovery that the familiar "muriatic" acid was not a compound of oxygen showed that the part played by that element in determining acidity was less than at first supposed. The acid, together with its allies from

the other members of the halogen group, were designated as "hydro-acids," a term still in vogue, through the prefix "hydro" in their names.

As the knowledge of structural composition of compounds developed, it became evident that it is not either hydrogen or oxygen that determines acidity but a particular association of these elements with reference to each other as well as to the rest of the molecule. During the middle period of the last century the electrochemical theories of Berzelius dominated chemistry very largely, and the vast majority of reactions were explained on the principle of attractions by positive and negative elements. Faraday's work contributed very much to the extension of these views. Later, the electrochemical theories fell into some neglect and were even mildly disapproved, but at present they have come into active application. The introduction and wide acceptance of the ionization theory has contributed greatly to this shift of opinion and out of this theory and the researches that it has initiated, has accrued much information of value in biologic chemistry.

Hydrogen is the element of lowest atomic weight so far known. Although not at present taken as the unit for atomic weights—oxygen having some practical advantages in that respect—its atomic weight may for general purposes be considered as unity. In the modern conception of the atom it is regarded as containing a positive nucleus which constitutes all but a minute amount of its mass and one electron. Its volatility and small mass cause it to be labile, that is, comparatively easily driven from combination by other elements, and also to have a rather wide range of combination, associating itself with both noticeably negative and noticeably positive elements. The elements by which it may be displaced are determined by those with which it is associated. When in combination with negative elements, such as chlorine, oxygen and sulphur, it is displaced by positive elements; when in combination with carbon, as in a vast number of organic compounds, it is displaced by negative elements, such as chlorine and oxygen. The discovery that chlorine can readily substitute hydrogen in organic substances was, indeed, somewhat of a surprise to chemists in the period in which the Berzelian theories of electrochemical relations were in high favor, but the fact is not now so puzzling. As the knowledge of the composition and properties of acids increased,

oxygen ceased to be regarded as deserving of the claim on which its name is based, and hydrogen came to be regarded as the acidifying principle. The introduction of volumetric methods and the discovery of indicators more sensitive and precise than the vegetable colors that were at first used, brought about a more liberal interpretation of the phenomena of acidity, alkalinity and neutrality. It was recognized that the acid condition depends largely on the position of the hydrogen in the molecule, as noted above. In further development of correct ideas on these points, the theory of ionizatin came into play.

As with all developments in science, it is difficult to find the point of origin of this theory. Wilhelm Pfeffer, a botanist, studied the phenomena of diffusion of organic liquids, such as sugar solutions, through membranes to elucidate some of the laws of vegetable physiology; Dutrochet carried the investigations further and introduced the terms "endosmose" and "exosmose," and Graham made a long series of experiments elucidating some of the laws of these transudations, and also discovered that differences of physical conditions, which he distinguished by the terms "crystalloid" and "colloid" determined marked differences in the power to pass through membranes. He invented, in fact, a new method of separation of compounds, which he termed "dialysis," which has found extensive application in physical chemistry. The studies of the phenomena of solution that are included in the labors of Pfeffer, Dutrochet and Graham were made almost entirely with water as the solvent, and inasmuch as this is the liquid which functions in all normal biologic processes, the data derived from such studies have direct reference to such processes. It will not be necessary, therefore, to consider the effects of any other solvent. When any solid substance is dissolved in water, the properties both of solvent and solvend are modified. The solution has a higher boiling point and lower freezing point, and lower vapor pressure than pure water. It has also a strong tendency to flow through a membrane into water on the other side or even into water in direct contact. Water in contact with water of the same composition, of course, does not have any tendency to exchange, but if one portion contains, for instance, sugar, this solution at once tends to penetrate the mass of the pure water. This "urge" is termed "osmotic pressure." Osmotic pressure bears a definite relation to the amount of the sub-

stance in solution, and also to its molecular weight, and the same is true of the change in boiling point, freezing point and vapor pressure. The molecular weight of urea is 60; of cane sugar, 342. The weights, respectively, dissolved in equal volumes of pure water, will give the same osmotic pressure, and many other examples of this might be given. It was found, however, that many compounds, salts, strong acids and strong bases, give osmotic pressures much higher than the rule just given requires. Sodium chloride has about twice the pressure; sulphuric acid about three times that which would be expected from the experiments with sugar and urea. The explanation of these exceptions is that by solution in the water, the acids, bases and salts have been modified so as to increase the number of active molecules, without producing an actual decomposition. It is held that in the case of sodium chloride, for instance, a considerable number of the molecules have acquired electrical charges, distributed among the atoms, so that all the sodium atoms so affected are positively charged, and all the chlorine atoms negatively charged. In modern theories, the arrangement of the atoms of sodium chlorine when in crystalline form is not regarded as simple pairing, but is more complicated, but when in solution it may be, and generally is, assumed that each sodium atom has a chlorine atom as a companion. Except in very dilute solution, some of these molecules escape the assumption of electric charges, and the extent to which such assumption takes place affects very markedly the properties of the liquid. The assumption of electric charge is termed "ionization," the charged elements being termed "ions." The word is derived from a Greek word meaning "to wander or travel," because such charged elements pass to one or other of the poles of an electric circuit. As only two electrical conditions exist, termed, respectively, positive and negative, indicated usually by the signs + and —, it follows that in compounds containing more than two elements, one at least of the ions must be compound. In hydrochloric acid, for example, all the hydrogen atoms may assume a positive charge and all the chlorine atoms a negative one, and if all the molecules in solution suffer such modification, the acid is said to be completely ionized. In nitric acid, however, there are three different elements and the distribution of these is $\overset{+}{H}$, $\overset{-}{NO_3}$. In ammonium nitrate we may have $\overset{+}{NH_4}$, $\overset{-}{NO_3}$.

The great practical, as well as theoretical, importance of these transformations is in reference to the action of acids and bases on living tissue. So far as their ordinary action upon non-living substances is concerned, ionization has comparatively little importance. It determines, it is true, the electric conductibility of liquids, whether produced by solution or by melting, for unless charged ions are present there is nothing to carry the current. Among the most important and frequent applications of acids are those for dissolving substances and neutralizing alkalies. In the latter application it has long been customary to employ solutions of equivalent —not equal—strength, termed standard solutions, the amount of acid present in a given volume being dependent on the molecular weight and the amount of hydrogen in the molecule *capable* of ionization, but not that which is actually ionized, for the extent to which ionization takes place is determined by dilution and by other circumstances. Each acid has its special susceptibility to ionization under given conditions. It has already been pointed out that the acid property depends on the manner in which the hydrogen is associated in the molecule. In sulphuric acid, for instance, both hydrogen atoms are united with oxygen, and both may assume electrical charges and be displaced by other positive elements which will combine with the oxygen. In acetic acid, however, although there are four hydrogen atoms, only one is directly associated with oxygen, the others being solely in contact with carbon. Hence acetic acid can yield but one positive ion for each molecule.

Another point of great importance is the susceptibility of each acid and alkali to suffer ionization at a given dilution. Great difference exists in this respect between the known acids and alkalies, and upon this depends largely the so-called *strength* of the substance. Sulphuric, nitric and hydrochloric acids are commonly termed "strong" acids; sodium hydroxide and potassium hydroxide are commonly termed "strong" alkalies, while acetic acid and ammonium hydroxide are said to be "weak." The distinction depends on the fact that at moderate dilution the strong acids and alkalies undergo extensive ionization so that a large proportion of their molecules are in a labile state and can act readily, while the weaker members of these groups are ionized to only a slight extent. Sulphuric, nitric and hydrochloric acid in moderate dilution in water have almost all their molecules in the ionized state, while acetic acid has but a small percentage in that condition. Similarly, po-

Epigæa repens, in nature. Acid soil. (Photographed by Clarence R. Shoemaker.)

Courtesy of the Franklin Institute.

Epigæa repens. Grown in pot with acid soil. (Grown and photographed by Frederick V. Coville, U. S. Department of Agriculture.)

Courtesy of the Franklin Institute.

tassium and sodium hydroxides in solution have a large proportion of the molecules ionized while ammonium hydroxide is affected to but a limited extent.

Of late years much investigation has been made of the relation of hydrogen-ion concentration to the growth of living organisms. In earlier studies in this field "total acidity" was mainly determined, but, as the statements made above show, this is not the factor that is most important. It has been found, for instance, that different species of some of the smaller animal organisms that live solely in water, select certain degrees of H-ion concentration. So it has been found that plants are influenced very materially by the H-ion concentration of the "soil solutions," that is, the water in the soil and the substances in solution therein. This phase of soil chemistry is comparatively new, and indications are that it may affect very seriously the existing theories of soil fertility and, indeed, relegate to the scrap heap a great deal of the data in agricultural chemistry that has been so assiduously gathered during the last fifty years or so. Soil analysis has been pursued very actively, and large amounts of money have been expended both in public and private laboratories. The United States Department of Agriculture has published many large volumes of maps and text, giving results of such analyses in various parts of the country. Except possibly pastoral life, agriculture is the oldest systematic human employment and for many centuries was conducted by empirical methods, mixed with not a little superstitution. Isolated and imperfect experiments were made from time to time, in the centuries that followed immediately after the revival of learning, but the practical ignorance of the composition of the air and the lack of correct methods of soil analysis prevented valid conclusions. Van Helmont weighed and planted a small tree in a tub, having also weighed the earth therein. He watered the earth regularly, and after the tree had grown considerably, he weighed it and the earth, and finding a notable increased in the weight of the tree inferred that water had been converted into plant tissue. He, of course, overlooked the carbon taken up by decomposition of the carbon dioxide of the atmosphere.

A little before the middle of the last century, Justus Liebig presented before the British Association for the Advancement of Science, an extensive report on organic chemistry in its relation to

agriculture and physiology, which appeared somewhat later in English as "Agricultural Chemistry." In this he discussed the assimilation of the forms of plant food, and developed very extensively the general principles on which the study of plant nutrition has been pursued. He disapproved of the view that the emission of carbon dioxide by plants in darkness is a process of respiration, attended by a corresponding absorption of oxygen, and his attitude on this matter prevented the acceptance of this view for many years. A long-established doctrine of agriculture is that the fundamental condition for nutrition of plants is a supply of carbon, nitrogen, potassium and phosphorus in such combinations as can be easily absorbed and diffused through the plant tissue. The carbon is derived principally from the carbon dioxide of the air, the nitrogen can be satisfactorily obtained from ammonium compounds or nitrates, the potassium and phosphorus from the soluble compounds of these elements. Continued experimenting showed, however, that many accessory conditions are influential, and the list of ingredients necessary to make a soil fertile is being continually expanded. Bacteriology came into the question. The soil under ordinary conditions is very rich in this type of organisms and they play a much more important part than was formerly supposed. They transform both organic and mineral matter into forms readily assimilable by plants.

The data available at present concerning the relation of hydrogen-ion concentration is very extensive, even though the subject is comparatively new. The processes for determining the degree of concentration of the hydrogen-ion in a given liquid are of two types. For exact determination and fundamental research electrolytic methods are used, which involve a very elaborate form of apparatus and much care in conducting experiments. Fortunately, a series of synthetic colors has been prepared which, by marked change, indicate approximately all ordinary degrees of ionization of acids and alkalies. With solutions of such colors, experimenters may make close approximations to the ion concentration of animal secretions and excretions, soil solutions and fluids of vegetable structures. The colorimetric method has been extensively applied for study of wild flowers in their habitats. Among American investigators, Dr. Edgar T. Wherry, of the United States Bureau of Chemistry, has been very active and has accumulated a large amount of interesting and valuable data. The general method has been

Shortia galicifolia, growing in neutral soil in the garden of Doctor Wherry, Washington, D. C.

Courtesy of the Franklin Institute.

Shortia galicifolia, the same plant as in the upper plate, but after growing for one year in subacid soil. (Both illustrations from photographs by Doctor Wherry.)

Courtesy of the Franklin Institute.

as follows: Small portions of soil close to the root of a given plant are mixed with pure water and after a short time has been allowed for the materials to mingle, a clear portion is tested on an ordinary spot-plate. The method is convenient and likely to be more accurate than transportation of the soil samples to the laboratory.

The investigations so far made along this line in different parts of the world show a fair degree of unanimity with a great number of plants and in very different regions, indicating that each species has its reaction preference, growing to best advantage in certain condition of ion concentration. Incidental points of value to agriculture are foreshadowed by some of the data obtained. Thus, it has been found that the potato can grow in a soil that has a reaction inimical to one of its parasites, so that by maintaining the favorable reaction the potato will grow but not its injurious associate. It must, however, be borne in mind that under the operation of the law of natural selection, strains of this parasite may be developed more and more resistant to a certain reaction and thus, ultimately, the potato may not be so easily protected. This phase has already been noted in relation to the boll-weevil, which is essentially a subtropical insect, but since its extensive spread through the cotton belt, it has been noticed that, at the northern border, forms of the insect are developed which have a higher resistance to cold than the parent strain. Some plants show indifference to the soil conditions in this respect. Whether this is due to specific differences not evident in the morphology, cannot be said. We must not overlook the fact that the soil is not merely a storehouse of food which the plant absorbs, but a collection of organisms which are sensitive to the soil-solution. Extensive investigation shows that highly acid or alkaline soils or those charged heavily with neutral salts will interfere with many plants. The distinction between marine and fresh-water floras emphasizes this fact strongly. Farmers have long known that excess of acid phosphate will produce a "sour" soil and do injury. In general, bacterial organisms thrive best in a slightly alkaline medium, and most catalysts are also similarly affected. The fertility of limestone soil has been long known. Ordinarily, the acids of the soil are produced by the decomposition of leaf structure. Carbonic acid is one of the products of this decomposition and plays a great part in the changes that take place in soils.

The amount of hydrogen ionization in a given solution is expressed generally by a system of symbols, which at first seem somewhat complicated, but are regarded favorably by most workers in the field. The exact form of the symbol differs considerably in different countries, but American workers have generally agreed on the form pH. The starting-point of the concentration is 1 gram of hydrogen-ion in 1000 cc. of water. Distinction must be noted between this and the conditions in an ordinary "normal" (N/1) solution. In the latter there is 1 gram *ionizable* hydrogen in 1000 cc., but it is not all *ionized.* Starting with this hypothetical normal solution of ionized hydrogen, successive dilutions by ten are indicated by exponents attached to the symbol pH, but these exponents are the logarithms of the quantities and not the direct expressions of the quantities themselves. The successive dilutions being the production of liquids containing less and less of the hydrogen-ion, the logarithms are minus, but the minus sign is not expressed, hence the somewhat puzzling fact that as the ion concentration diminishes the exponent increases. The following table shows the method of applying the symbol.

Amount of Ionized Hydrogen in 1000 cc. of Water		Proportion to Unit Standard	Actual Logarithm	Symbol as Written
1	gram	1	0	pH_0
0.1	"	0.1	—1	pH_1
0.01	"	0.01	—2	pH_2
0.001	"	0.001	—3	pH_3
0.0001	"	0.0001	—4	pH_4
0.00001	"	0.00001	—5	pH_5
0.000001	"	0.000001	—6	pH_6
0.0000001	"	0.0000001	—7	pH_7

The last concentration is 1 gram of ionized hydrogen to 10,000,000,000 cc. (ten billion cc.). (This is the American and French method of notation of the higher numbers; in Great Britain a billion is a million millions.) This quantity of ionized hydrogen is that which occurs in pure water under the influence of its own ionizing power, so that pH_7 represents neutrality. The concentration of the hydrogen-ion cannot be brought below this proportion in any solution except by the counteraction of hydroxyl. In the pH_7 there is, of course, the status H, HO, the two ions being chemically equivalent, but representing, respectively, 1 and 17 parts by weight. To reduce the hydrogen-ion concentration below pH_7, hydroxyl may be added in the form of one of the soluble hydrox-

ides, such as KHO, NaHO or NH_4HO. The extent to which the pH will be increased will depend upon the ionizability of the substance added. Sodium and potassium hydroxide will show stronger pH than ammonium hydroxide in equivalent amount, but it must again be noted that the *total alkalinity*, as determined by titration with acid, will be same 56 1 of KHO, 40 of NaHO and 35 of NH_4HO in the same volume of pure water will require the same amounts of acid to neutralize, but will not give the same ion concentration by either the electrical or colorimetric method.

pH	Specific Acidity	pH	Specific Acidity	Specific Alkalinity
4.0	1000	7.0	1.0	1
.1	800	.1	0.8	1.25
.2	630	.2	0.63	1.6
.3	500	.3	0.5	2
.4	400	.4	0.4	2.5
.5	315	.5	0.32	3.15
.6	250	.6	0.25	4
.7	200	.7	0.2	5
.8	160	.8	0.16	6.3
.9	125	.9	0.13	8
5.0	100	8.0	0.10	10
.1	80	.1	0.08	12.5
.2	63	.2	0.063	16
.3	50	.3	0.05	20
.4	40	.4	0.04	25
.5	31.5	.5	0.032	31.5
.6	25	.6	0.025	40
.7	20	.7	0.02	50
.8	16	.8	0.016	63
.9	12.5	.9	0.013	80
6.0	10	9.0	0.010	100
.1	8	.1	0.008	125
.2	6.3	.2	0.0063	160
.3	5	.3	0.005	200
.4	4	.4	0.004	250
.5	3.15	.5	0.0032	315
.6	2.5	.6	0.0025	400
.7	2	.7	0.002	500
.8	1.6	.8	0.0016	630
.9	1.25	.9	0.0013	800
7.0	1	10.0	0.0010	1000

Owing to the comparative awkwardness of the pH symbol, due originally to Sörensen, Wherry has suggested an entirely different method of statement, beginning at neutrality and indicating the ion concentration by multiples for acidity and decimals for alkalinity. "Specific acidity," the term used in this direct method, is the amount of hydrogen-ion in 1000 cc. of a given solution expressed in terms of the (approximate) ion concentration of pure water

(1 gram in 10,000,000,000 cc.). "Specific alkalinity" is the corresponding amount of equivalent hydroxylion. As it is often desirable to make comparisons between the two systems, or conversions of one into the other, Wherry has prepared a table which is herewith transcribed from *Ecology* (1923, *3*, 346). The original suggestion appeared in *Jour. Wash. Acad. Sci.* (1921, *11*, 197).

Doctor Wherry has favored me with a number of illustrations of plants growing in special conditions of hydrogen-ion concentration, the conditions having been ascertained by the colorimetric

Asplenium montanum. Acid soil. (Photograph by Clarence R. Shoemaker.)

Courtesy of the Franklin Institute.

methods above mentioned. Among the interesting data thus obtained is the fact that the familiar rhododendron will thrive only in a distinctly acid soil. Already soil-analysis by this method has resulted in securing valuable data as to the adaptability of certain districts to certain kinds of plants.

Several forms of apparatus for the employment of the colorimetric methods have been devised. The electric methods are difficult and involve the use of expensive apparatus. A universal indicator of considerable range of sensibility was described by F. H. Carr in the *Analyst* (1922, *74*, 196). This is a mixture of several

colors, and curiously, the color changes follow the spectrum order, the lowest pH to which the indicator is sensitive producing red and the highest violet. I have tried this indicator and found it in the main satisfactory. A difficulty is that methyl-red, which is one of the ingredients, is somewhat unstable and the colors produced in the intermediate pH values are apt to be less pronounced than desirable. The solution keeps pretty well, however, for several months and seems to be adapted to field work. For the use of individual colors, the "Double-wedge Comparator" made by Sterlin, of New Haven, Connecticut, is convenient, and has been much used by Doctor Wherry, who has suggested some details in its construction.

It must be borne in mind that the reaction to colors or even the conductibility of a solution may not tell all about the effect of given ion concentration. The other substances in the liquid may take active part. It has recently been shown that while a 4 per cent. solution of acetic acid will corrode stainless steel, a malt vinegar of the same strength will not, and the same is true of a 4 per cent. pure citric acid solution as compared with the same strength of lemon-juice. The "buffer" effect of the other organic matters present is probably responsible for the difference.

In conclusion, I wish to express my obligations to Dr. Edgar T. Wherry for much assistance in the preparation of this paper, loan of slides, original photographs and literature on the subject.

BRONCHIAL ASTHMA AND OTHER ALLERGIC MANIFESTATIONS IN PHARMACISTS.*

By M. Murray Peshkin, M. D., New York.

There is a considerable accumulation of data in the literature on occupational idiosyncrasies, but comparatively little has been written concerning pharmacists and their tendency to acquire protein sensitization to the organic preparations that they handle. In view of the widespread interest that has been aroused by the subject of allergy and asthma in general and the ever increasing volume of literature on this subject, the scarcity of reports dealing with the subject under discussion is indeed surprising.

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Idiosyncrasy following the ingestion of various drugs has been observed and discussed since the early days of medical science. This paper, however, deals only with the allergic manifestations due to contact with and inhalation of drugs.

In 1920, I [1] reported a case of true anaphylactic bronchial asthma in a pharmacist, aged twenty-nine, due to the inhalation of powdered ipecac engrafted on a recurrent seasonal bronchitis. Skin tests performed with the many drugs in powder form commonly used were negative, except pulvis ipecacuanhae et opii (Dover's powder), which gave a positive reaction. Powdered opium, ipecac and lactose—the constituents of Dover's powder—were then tried, giving a positive reaction only to ipecac in as weak a dilution as 1 : 100,000. The ingestion of ipecac produced no ill effects referable to the respiratory tract.

Widal, Abrami and Joltrain,[2] in 1922, reported two cases of ipecac sensitization in pharmacists. Contact with emetin induced eczema in a main, aged thirty-four, and handling ipecac induced asthma in a man of fifty-five.

Bernton,[3] in 1923, cited a case of sensitization to the protein of castor bean in a chemist, aged twenty-seven, who was engaged in a "drug and plant oil investigation" in the United States Department of Agriculture. Exposure to the dust of the castor bean was followed by itching of the eyes, lacrimation, sneezing and rhinorrhea, ending in an attack of asthma. A cutaneous reaction was obtained with a drop of the protein solution of the fat free castor bean in a dilution of 1 : 250,000. Of five other persons engaged in the same work and exposed to castor dust, only one showed a tendency to sneezing. The cutaneous reaction in all these cases was negative.

The preceding case reports seem to be the only references in the literature dealing with this subject. Urged by an impression that allergic symptoms in persons engaged in pharmaceutic and kindred professions are not as infrequent as one is led to believe from the literature, a questionnaire was sent to fourteen manufac-

[1] Peshkin, M. M.: "Ipecac Sensitization and Bronchial Asthma," *J. A. M. A., 75:* 1133 (Oct. 23), 1920.

[2] Widal, F.; Abrami, P., and Joltrain, E.: "Anaphylaxis to Ipecac," *Presse méd., 30:* 341 (April 22), 1922.

[3] Bernton, H. S.: "Occupational Sensitization to the Castor Bean," *Am. J. M. Sc., 165:* 196 (Feb.), 1923.

turing pharmaceutic houses to determine the possible incidence of sensitization in this professional group. The questions were as follows:

1. Have any cases of asthma, coryza, lacrimation, spasmodic cough, eczema or urticaria come to your attention that could be attributed to the inhalation of, or contact with, ipecac, lycopodium or rhubarb?

2. Have any other drugs (synthetic or of plant origin) or animal extracts been known to cause any of the conditions or symptoms enumerated?

Answers were received from all. Four concerns reported workers suffering with asthma due to inhalation of ipecac and others suffering from urticaria due to contact with emetin solution. One of the largest manufacturers of pharmaceuticals wrote that:

> The physician in charge of our hospital advises that he has had yearly upwards of 100 calls for services where patients were suffering from bronchial asthma or other evidences of respiratory irritation from dust, chiefly resulting from grinding ipecac. Despite our efforts to confine dust in grinding ipecac, the particles would get in the air and affect susceptible individuals at considerable distances from the grinding room. We have finally been able to control the trouble from grinding ipecac, until we have now only a few patients who ever come in sufficiently close contact with the drug to experience any trouble.

Another firm said that one worker had been forced to leave the laboratory whenever ipecac preparations were being handled, on account of acute asthmatic attacks. A third house reported twelve cases of sensitization to emetin solution. These cases were characterized by urticaria of the forearms and hands, with intense itching.

No cases were reported of affection from exposure to powdered rhubarb or lycopodium.

Next to ipecac, the most common causes of asthma are poke root and podophyllin. One firm said:

> We have experienced some trouble with podophyllin and poke root in causing bronchial asthma, but these cases do not exceed probably half a dozen cases from each drug a year.

Three workers suffered from vanillism from handling vanilla beans, with symptoms similar to those noted in the cases in which there was sensitiveness to emetin. One worker showed sensitivity by inhalation to urease, which is derived from the jack or soy bean.

Two firms reported that several persons were transferred from the drug milling and grinding room, on account of sensitiveness to certain powdered drugs. The fact that quite a variety of drugs were handled made it impossible to trace, with any degree of exactness, the causes of asthma in these persons.

Powdered bile salts are somewhat irritating and the workers generally wear respirators, but no cases have occurred in which allergic symptoms were manifest.

Numerous skin irritations from a variety of synthetic chemicals were noted, but no instances of asthma have occurred in the workers following inhalation.

While all the concerns prepared various glandular extracts, four of these were almost entirely devoted to this field. It appears that the workers who handle the desiccated glandular extracts experience no inconvenience. They do not even wear respirators as a rule. However, one firm wrote that:

> Epinephrin crystals is the only animal extract noticed to cause any discomfort to our workers; it is very irritating to the mucous lining of the nostrils and the esophagus.

Another wrote that:

> In the manufacture of pancreatic products there is frequently observed an erosion of the mucous membrane of the nose and throat and of the epidermis of the finger tips. This is attributed to the presence of the active proteolytic ferment contained in the products. We have, of course, developed a means to meet this situation.

It is well known that in an asthmatic subject an attack may be induced purely by mechanical irritation. It is possible that some of these preparations, such as bile salts and epinphrin crystals, which our correspondents mention, may excite asthmatic attacks by mechanical irritation, and these attacks should not be confused with cases of specific hypersensitiveness. These cases can be classified and differentiated by the skin tests. If this procedure was

carried out in all such cases, greater progress could be made toward their classification and proper management.

A careful search of the literature covering a period of 100 years fails to show any case of bronchial asthma or hay-fever caused by powdered rhubarb or lycopodium. Therefore the following case reports will be of interest, since they demonstrate unusually rare types of protein hypersensitization in pharmacists.

Report of Cases.

CASE 1.—An unmarried man, aged twenty-seven, employed as a prescription pharmacist for the last nine years, the details of whose case report were kindly furnished me by Dr. S. P. Holland, Blakely, Ga., soon after he began handling drugs was seized at irregular intervals with typical symptoms simulating hay-fever. These symptoms occurred only when the patient was working in a drug store, and were relieved when he was off duty or unemployed. It was not until the summer of 1922 that the patient became definitely certain that the handling of powdered rhubarb, or exposure to it, was responsible for his perennial hay-fever. The past and family histories were irrelevant.

Physical examination was negative. Aug. 24, 1922, Dr. Holland performed protein skin tests against rhubarb. The skin reaction appeared within one and one-half minutes, presenting a wheal 18 mm. in diameter and surrounded by an intense erythema.

CASE 2.—I. T., a man, aged twenty-six, a student at Fordham University School of Pharmacy and employed as an apprentice in a drug store since 1916, referred to me by Dr. Jacob Diner, New York, had enjoyed good health until the fall of 1918, when he was first entrusted with the preparation of certain pills in which lycopodium was used as a dusting powder. During the first handling of lycopodium, he was seized with violent sneezing, lacrimation and rhinorrhea, ending in an attack of asthma. These symptoms were not relieved until half an hour after he left the store. He recalled that during the two years prior to the actual handling of lycopodium he had frequent sneezing spasms of short duration while working about the store. Following a second but more severe attack of bronchial asthma, one month later, every effort was made to avoid exposure to lycopodium. However, soon after this he desired to convince himself that lycopodium was actually responsible for the

bronchospasms, so on several occasions he intentionally exposed himself to the powder. Each exposure resulted in severe asthmatic seizures. Later on, the patient observed that even the handling of lycopodium by another person while he was in the same room always induced a bronchspasm, and that he thereby averaged about two dozen attacks yearly. In 1922, he matriculated in the school of pharmacy. After he had an attack of asthma in the laboratory, the use of lycopodium in the school was forbidden, and he remained free of all symptoms for one year. October 22, 1923, lycopodium was again used in the laboratory. He was in the third section; two previous classes had employed lycopodium that day. On entering the laboratory, he was immediately seized with the most violent attack of asthma he had ever experienced. This bronchospasm was of two hours' duration. For the following three days he had mild recurrent bronchospasms, with respiratory oppression and wheezing during the intervals of attacks. In the last year, his tolerance for lycopodium had become so lowered that the mere entering of a room in which the powder was employed resulted in a very severe attack of asthma.

Recently, he had observed that the ingestion of mustard caused respiratory oppression and wheezing for several hours, and that exposure to a cat caused merely sneezing. A positive skin reaction to desiccated extract of pancreas revealed the fact that the handling of this drug caused sneezing. During the intervals of asthmatic attacks, the patient was entirely free of all symptoms. The past history was irrelevant, except that the patient's tonsils and adenoids were removed in 1914. A nasal operation was performed one and one-half years after the first bronchospasm, without affording the slightest relief. The family history was negative.

Physical examination was negative. The patient was of excellent physique. Skin tests were performed with many drugs in powder form; the reactions to desiccated gland extracts were negative, except lycopodium and the extract of pancreas, which gave positive reactions. The reaction to the lycopodium powdered protein presented a wheal of 12 mm. with an intense erythema of 4 cm. The patient reacted to a dilution of 1 : 100,000. The reaction to the desiccated extract of pancreas presented a wheal of 8 mm. with an intense erythema of 3 cm. He reacted to a dilution of

1 : 100. These drugs were not orally administered for the purpose of observing their effects because of the patient's unwillingness to submit to such a test.

Cutaneous tests against 116 food, bacterial, pollen, epidermal and dust proteins resulted in plus minus reactions to cat hair, mustard and banana.

Conclusion.

1. Sensitization to drugs is more common than one is led to believe from the few reports in the literature.

2. Ipecac is the most common cause of bronchial asthma in pharmacists and pharmaceutical workers.

3. Next to ipecac, the commonest causes of bronchial asthma in pharmacists are podophyllin and poke root.

4. The handling of emetin solution and vanilla beans causes skin manifestations characterized by urticaria of the forearms and hands, with intense itching.

5. Synthetic drugs and desiccated animal gland extracts apparently play no role in the causation of bronchial asthma, except that by inhalation they may induce an asthmatic attack by mechanical irritation.

6. Rhubarb and lycopodium hypersensitiveness are unusual causes of allergic manifestations in pharmacists.

7. The occupations of pharmacist and pharmaceutical worker and their relation to bronchial asthma and other allergic manifestations due to drugs is an important one, it would appear, and deserves more attention.

562 West End Avenue.

MEDICAL AND PHARMACEUTICAL NOTES

Moissan Prize Endowment.—Louis Moissan, son of the distinguished chemist, lost his life in the French army in August, 1914. His will provided for the presentation to the School of Pharmacy in Paris of the apparatus used by his father in the fluorine researches, and also an endowment of 200,000 francs for awarding two prizes to students of the school, one to be in name of his father and the other of his grandfather. War conditions delayed the development of the endowment, and then the heirs brought suit. The litigation was terminated in April last by a decision in favor of the faculty of the school.

Poisoning by Haarlem Oil.—Since the middle ages, Haarlem Oil has enjoyed wide popularity as a medicine, almost as a cure-all. In the *Schweiz. Apotheker-Zeitung* (1924, *63*, 327) a fatal result from overdose is recorded. The composition is by no means uniform. In many places it consists of oil of turpentine, sulphur and juniper oil; elsewhere it may consist of balsam of sulphur, poppy and olive oils and other ingredients. In France, it is mostly a mixture of Dippel's animal oil and oil of turpentine, sometimes with the addition of camphor. It has especially wide popularity as a remedy for toothache. It was in the use of it for this purpose that the fatal accident occurred. A girl of sixteen, in good health, complaining of severe toothache was given two vials of the oil, amounting to about 10 cc. each. Instead of taking about a gram, which was the dose prescribed on the label, the girl took the contents of one vial. This was during the night when she was alone in her sleeping room and other members of the family were in bed. In the early morning the family were awakened by the condition of the girl who soon after died. The cause was suffocation due to the action of the oil upon the respiratory tract. The German reporter observes that it is most remarkable that even in these days of widespread information so many persons should still believe in the cure-all properties of the oil. H. L.

Bottled Carbonated Waters.—The so-called "soft drinks," are a striking feature of American life, and the establishment of retrictions on the use of alcoholic beverages has tended to increase the use. The industries now directly and indirectly concerned with the manufacture and sale of these beverages are enormous in extent and have been well-organized under expert engineering and chemical control. Some idea of the nature and methods of such industries will be gained by a visit to the exhibitions at the annual convention of the American Bottlers of Carbonated Beverages at Louisville in November next. The production of carbonated beverages is a very old industry, but in the beginning everything was done by hand; now every step of the procedure is conducted by machinery and human hands do not touch the product at any point.

The first "soda-water" seems to have been made by Joseph Priestley. Townsend Speakman, a Philadelphia druggist, in 1807, flavored this with fruit juices, and thus originated the carbonate beverage. At present a research laboratory at Iowa State College has been endowed by the A. B. C. B. as the national association mentioned above is generally known. Federal statistics show that about eight billion bottles (6½ fluid ounces, slightly less than half-a-pint) were consumed by the American people last year. It is calculated that the contents will amount to five hundred million gallons, which is nearly five gallons for each inhabitant in the country.

H. L.

A New-Idea Pharmacy Society.—A recent issue of *Jour. Pharm. Chim.* states that a society of pharmacists with large families has just been founded in France. The French people have been greatly worried of late years concerning the declining birthrate, especially in view of the high rate east of the Rhine. The society will be devoted to mutual aid, and to help support the families when the breadwinner has died or has become unable to furnish support.

H. L.

SCIENTIFIC AND TECHNICAL ABSTRACTS

Qualitative Distinction Between Vanillin and Cumarin.—In the course of some investigations on tests for acetone, formaldehyde and acetaldehyde, two reactions of distinction between these well-known flavoring agents were noted. If a dilute solution of acetone is mixed with a dilute solution of vanillin, and a fragment of solid sodium hydroxide dropped in, the liquid shows very soon a yellow ring around the alkali, which changes to a marked red. Cumarin produces no effect. If a solution of hydrazin sulphate is added to a solution of vanillin, a yellow tint at once develops and deepens appreciably on standing. Cumarin gives no color.

H. L.

Physiologic Actions of Tonka Bean.—The bean of the *Dipterix odorata* Willd., is well known as a cheap flavoring agent, especially as a substitute for vanilla. E. Roquette-Pinto communicates to the *Bulletin of the National Museum of Rio Janeiro* a report of some studies of the effects of internal administration of the drug. The publication is a new venture, the article appearing in the second issue (*Bol. d. Museu Nacional d. Rio Janeiro*, 1924, *I*, 127). The author gives a good deal of data about the plant, its product, and methods of extraction of cumarin. His experiments were made largely on frogs. He finds the action of two kinds: on the cerebrospinal system indicated by anesthetic effects and also directly on the cardiac nerve centers, disturbing the rhythm of the muscular action.

H. L.

Alcohol as a Motor Fuel.—Fuel is king. No greater striving of the nations is to be found at present than that for control of the fuel supplies of the world. For many years coal has been the objective point, but the urge has now shifted, and oil is the desired material. In connection with the development of the combustion motor, the possibility of using alcohol in whole or part has been prominently before engineers for some time. Each nation of importance is anxious to have within its own territory sufficient fuel supplies, and as the deposits of coal and oil are not distributed

equally, investigations are being made to secure such materials as can be produced at will. Alcohol is practically inexhaustible. Starch-containing plants can be grown in unlimited amount and the fermentation is a simple process. Up to the present time the cost of such manufacture has been so far above the cost of standard motor fuels that the alcohol motor has been only suggestive.

France is one of the nations that has taken alarm as to the source of volatile fuel, and elaborate experiments have been undertaken to determine how far a mixture of alcohol and common hydrocarbon fuel can be made practicable. A report on results so far attained appears in the *Ann. d. Chim. Anal et Appl.* ([2], 1924, *6*, 136) prepared by George Baume. It has been found that absolute alcohol is much better suited for admixture with the hydrocarbons than when water is present. With the absolute form about equal parts of the two liquids can make a stable mixture. Some adjustment of the motor is needed to secure efficient service, but this problem has been solved. It is claimed that the alcoholized fuel is less likely to produce knocking.

The manufacture of an alcohol containing only traces of water by the ordinary method is an expensive process. The committee investigating the matter has adopted a method devised by Sydney Young and used in certain French distilleries. It consists in rectifying the alcohol in the presence of benzene. The distillate consists of benzene, water, and a small quantity of the alcohol; the greater portion of the latter remains in anhydrous form in the still. Operations of this character have been carried on to the amount of several thousand gallons per day. The problem of the denaturing of this alcohol has also been considered. H. L.

Asbestos and Mercury in 1923.—The production of asbestos in 1923 was 310 short tons to the value of nearly $25,000. This, although larger than the output of 1922 is far below that of some previous years. The source is principally chrysotile, all of which is mined in California and Arizona.

The mercury production also improved in 1923, California furnishing 69 per cent. of the total United States output. The price declined considerably during the past year, but early in the present year improved notably. If a price of about $70 per flask can be maintained, a further increase of output is probable. A new mercury boiler designed by W. L. R. Emmet is about being tried and

if it is as successful as its promoters believe, an increased demand will develop, but this is not expected immediately. Should the invention become actively used, mercury will have to be imported to supplement the home supply. The above data are taken from a circular (17291) of the Department of the Interior, U. S. A.

H. L.

THE ITINERARY OF AN ABSTRACT, WITH NOTES ON THE SUBJECT-MATTER THEREOF, HENRY LEFFMANN.—About eighteen months ago, E. Wertheim of the College of Arts and Sciences, Fayetteville, Arkansas, communicated to the *Journal of the American Chemical Society* (1922, *44*, 1834), a modification of the preparation of Schiff's reagent for aldehydes. A description of the procedure with the results of tests of it will be found elsewhere. The present purpose is to show the progress of the suggestion through the journals, during which it suffered a serious "sea-change." Wertheim's article was duly abstracted in the *Journal of the Society of Chemical Industry* (1922, *41*, 790a) from which it was taken by an abstractor for the *Pharmaceutical Journal and Transactions* ([6] 1922, *55*, 401). It then crossed the Channel, and appeared in the *Repertoire de Pharmacie* ([3], 1923, *35*, 111). Like Napoleon, it passed across the Alps, and appeared in the *Bollettino Chimico-Farmaceutico of Milan* (1924, *63*, 312).

In the last abstracting, the directions were materially changed. The original article prescribed a solution of 0.005 gram of rosanilin hydrochloride in 300 cc. of water, but the Italian abstractor made it 0.5 gram. The incident shows the serious defects of the system now much in vogue, of secondary abstracts. It is true, and it is unfortunate, that local pride often leads to publication in journals or reports of limited circulation, but nations that pretend to prominence in science should have at their command the standard literature of all countries. Neither the French nor the Italian abstract refers to the original source, but both the British ones do. It is not necessary, however, that the entire genealogy of the abstract should be given, but each step should note the original reference. The French item, for instance, refers to *Pharm. Jour.* only. It should carry a brief allusion to the original source (which is given in the British abstract). A full reference would not be needed (*J. A. C. S.*, 1922) being enough to direct the chemist who desires to use the test, to the original source.

H. L.

RADIUM PRODUCTION IN 1922.—One of the most striking of the many striking features of development in mining and metallurgy in recent years is the discovery of large deposits of metals that were long very rare and without particular use. The employment of thorium and cerium compounds in the manufacture of the Welsbach mantle, was followed by the discovery of mines yielding the necessary ores in large amount. A somewhat similar course has followed the discovery of helium. Radium ores were scarce when the element was first recognized and the amount present very minute. The value of the material was so great not only from its rarity but from its unique properties that search was carried out industriously in all accessible regions. Considerable ore of fair quality was found in the United States, but it appears from the advance sheets of the "Mineral Resources of the United States for 1922" that American radium manufacture has been seriously affected by the discoveries in the Belgian Congo. Fasciculus I 27, which consists of pages 557 to 583 of the above-mentioned volume (issued by the United States Geological Survey) states that in 1921 the radium producers carried stocks so large (a few thimblefuls) that they were obliged to sell at little profit, and they started the year 1922 with over one million dollars tied up in radium salts and ore. The condition was made worse by competition with the very rich Congo ore. This was discovered in 1913, but the first lot was received at Antwerp in December, 1921. During the year 1922 a standard price of $70 per milligram was maintained. Works now operating in Belgium are said to have a capacity of three grams of radium per month in a salt containing about 95 per cent. of radium chloride. The copper deposits in northern Rhodesia are said to be continuous with those of the lower Belgian Congo, and the uranium ores may also be found in British territory. The pamphlet refers to the exploitation of waters exhibiting radio-activity, and states that whatever quality such waters may have at the springs, the bottled samples lose this activity in a few days.

The famous Joachimsthal mines in Bohemia are now part of Czechoslovakia, and the government of that nation is preparing to operate the mines. The total production of radium in the Joachimsthal region from 1911 to 1922, both inclusive, has been 22.3 grams.

H. L.

BOOK REVIEWS

A MANUAL OF URINE EXAMINATION FOR STUDENTS OF PHARMACY AND NURSING. By Florin J. Amrhein, Ph. G., Ph. C., Assistant Professor of Chemistry at the Massachusetts College of Pharmacy, Boston. 12mo. of 201 pages, with 50 illustrations. Philadelphia and London: W. B. Saunders Company, 1924. Cloth, $2.00, net.

This little volume represents a very determined effort to treat the subject of urinalysis from a very practical viewpoint. The effort has been eminently successful and the author has well avoided the superfluity of theory so often encountered in such works.

The book presents concisely the more important physical, chemical, micro-chemical and microscopic methods now generally used in urinary analysis. Its emphasis throughout is on practice and methods. The manual allows for necessary laboratory work in class study.

The illustrations, excepting the line cuts of casts and cylindroids are exceptionally good. It is very singular that most printed illustrations of the various casts are alarmingly unlike what really appears on the microscopic field. In that respect this book is no exception.

On page 74, referring to diabetic urine, the author writes "The amount voided in twenty-four hours is generally increased, *the color high.*" With the great majority of diabetic urines, the color is not high, but quite the contrary.

The author chooses thymol as the best preservative for urine and advises placing an amount equivalent to the size of two peas in the receiving bottle. So much thymol interferes with the ferric chlorid, diacetic acid test and in urines containing a mild trace of albumin it accentuates the Heller's test for that substance. Additionally, thymol is an article not generally available to the laity. Boric acid is far better for this purpose, for it interferes with no test, it is generally available and it costs very little.

These are unimportant exceptions, however, and it can be said quite correctly that this is a sensible, well-compiled little volume,

up-to-date in the choice of its several tests, careful in its interpretations and extremely accurate in its theorems and tabulations. It affords to the clinical chemist a very thorough and practical laboratory reference book.

Ivor Griffith.

The Physical Chemistry of the Photographic Process. A General Discussion held by The Faraday Society, London, May, 1923. 8vo, 406 pp. Limp cloth. 12 s. 6 d.

The present volume is another valuable addition to the scientific and educational "General Discussions" held by and then published by The Faraday Society of London. In time these different volumes will constitute a library by themselves.

The General Introduction was given by Prof. Wilder D. Bancroft, of Cornell University, and Editor of *The Journal of Physical Chemistry,* and dealt with "The Theory of Photography," which he divided into the emulsion, the latent image, and the development. The meeting consisted of four sections and the number of papers before each section is given in parenthesis: I. Physical Chemistry of the Vehicle and of the Emulsion (6); II. Reactions of the Plate During Exposure (4); III. Development and Characteristics of the Developed Plate (7); IV. Adsorption Reactions in Photographic Films (6).

Besides this a number of general discussions were held. The volume before us is an important contribution to the scientific as well as the technical side of photography. All those interested, which includes many pharmacists and chemists, should read and study this excellent book.

Otto Raubenheimer, Ph. M.

Chemical Synonyms and Trade Names. A Dictionary and Commercial Handbook. By William Gardner. Royal 8vo, 271 pp. Cloth. 25 s. Crosby, Lockwood & Son, Stationers' Hall Court, London, E. C. 4.

Just off the press, comes to us from the other side of the Atlantic this Dictionary of Chemical Synonyms and Trade Names. Ow-

ing to the various synonyms and trade names employed there exists at the present time considerable confusion in the chemical trade and also in pharmacy. It has been the object of the author, a practical "works chemist," to supply a ready reference book, a task which he has splendidly fulfilled!

The book is arranged strictly alphabetically, is thoroughly cross-indexed, is quite up-to-date and on 271 pages of two columns each, contains fourteen thousand definitions and cross-references. The short definitions in the book are a very valuable asset, f. i., "Fetid Spirit of Ammonia" (Spiritus Ammoniæ Foctidus, B. P.), an alcoholic solution of the volatile oil of asafetida mixed with a solution of ammonia. The definition of "Lager Beer," a beverage containing 3.5 to 4 per cent. alcohol, reminds us of the olden, gone-by days and makes our mouth water!

The scope of the book is quite exhaustive as it includes minerals, chemicals, drugs, dyes, pigments, explosives, alloys and materials in common use. The work is a very valuable reference book for importers, manufacturers, dealers, wholesale and retail druggists, chemists and last, but not least, pharmacists. We wish the book the best of success and predict a wide field of usefulness, also in the United States.

Otto Raubenheimer, Ph. M.

Potter's Cyclopædia of Botanical Drugs and Preparations. 3d Edition, 15th thousand. By R. C. Wren, F. L. S., With Additions by E. M. Holmes, F. L. S. 12 mo., 392 pp. Cloth, 5 sh. Potter & Clarke, Ltd., 60 Artillery Lane, London, E. I.

"The well-known virtue of vegetable drugs, well known and tried for centuries, was in the course of time ridiculed and forgotten. Medical science enthusiastically used mineral poisons, coal tar and aniline derivatives and synthetic chemicals for a while, until to their sorrow they discovered bad effects resulting from their use. Then again they took hold of the remedies of old, the herbs, roots, etc., and preparations therefrom." (Schelenz-Raubenheimer, A. J. P., Vol. 81, p. 115.)

Above quotation may serve well as an introduction to this book review. When a book is in its third edition and its printing is in the fifteenth thousand, it is verily a true proof of its usefulness and

popularity! The present volume contains nearly 3000 references and gives the uses, preparations, doses, synonyms and distinctive characters of all botanical drugs used in medicine. Many U. S. P. preparations are included and synonyms in both Latin and English are given. Prof. E. M. Holmes, of international reputation, has prepared the descriptions of the distinctive characteristics of each drug, a sure proof of their reliability. Another advantage of the present edition is the inclusion of 200 engravings of English herbs, drawn from nature by W. H. Fitch, F. L. S., and W. G. Smith, F. L. S., and taken from Bentham's "Handbook of the British Flora."

Besides all this the book contains an Index of Therapeutic Action, Forms of Medicinal Preparations, Doses and Their Equivalents, Continental Herbal Compounds, Glossary of Botanical Terms, Botanical Names and the Authorities for them, Abbreviations of Names of Botanists, and last but not least, an excellent Index to the Cyclopædia, giving the Common Names in Capitals, the Botanical Names in Italics and the Synonyms in Roman type, an innovation of which any book can be proud of.

Potter's Cyclopædia of Botanical Drugs and Preparations is a storehouse of valuable information. It is a ready reference for the busy pharmacist and should become better known in the United States. We can highly recommend this valuable and inexpensive book!

Otto Raubenheimer, Ph. M.

Poison Mysteries in History, Romance and Crime. By C. J. S. Thompson, M. B. E., Author of "The History and Romance of Alchemy and Pharmacy," etc., etc. 12 mo., 412 pp. 12 Illust. Cloth, $3.50. Philadelphia, J. B. Lippincott Co., 1924.

The author is a former pharmacist and now Curator of that great treasure house of pharmaceutical and medical relics, the Wellcome Historic Medical Museum at London. As early as 1899 Thompson published a smaller volume, "Poison Romance and Poison Mysteries," of which there was also a second edition. The present volume is an outgrowth and decided improvement on the former.

The book is divided into two parts.

Part I. Poisons in History and Romance. From its 26 chapters we will briefly mention the following: Poisons used by Ancients and Primitive Races; Poisons used by the Egyptians, Greeks, Romans, Hebrews, Chinese, Persians and Hindus. Antidotes to Poisons; Some Classical Poisons and their Histories; Royal and Historic Poisoners. The Italian School of Poisoners; Poison Cases in Different Countries; Love-Philtres and Poisons; Poisons Used in Warfare; Poisons in Fiction.

Part II. Poison Mysteries. From the 23 chapters we point out the following headings: The Mystery of Lawford Hall; the Case of Madame Lafargue; The Bravo Mystery; The Case of Dr. Pritchard and Dr. Lamson; Poison Mysteries in France; American Poison Mysteries; Some Irish Poison Mysteries; The Dalkeith Coffee Poison Case; The Armstrong Case.

From the 12 illustrations we want to call attention to the following ones: Natives of the French Sudan Preparing Arrow Poison; Drinking Cup of Unicorn's Horn; Bezoar Stones; Aqua Taffana Bottle; A Cup of Wine with Casare Borgia; Stethoscope and Pocket Medicine Case carried by Neill Cream

The author is to be complimented, not only for collecting an immense amount of material, but also for arranging it in his book in such a manner so as to make the contents interesting and instructive from beginning to end. Under "American Poison Mysteries" we want to call special attention to the celebrated Molineux case in New York City in 1899—Mercuric Cyanid in Bromo-Seltzer. This volume is the most remarkable and complete collection of poison lore. We can highly recommend the book to all interested and quote especially to chemists, physicians and pharmacists.

OTTO RAUBENHEIMER, Ph. M.

LEHRBUCH DER CHEMISCHEN TOXIKOLOGIE UND ANLEITUNG ZUR AUSMITTELUNG DER GIFTE. FÜR APOTHEKER, CHEMIKER UND MEDIZINER. Von Dr. J. Gadamer, Professor der pharmazentischen Chemie a. d. Universität Marburg. Zweite-vermehrte Auflage. Lexicon, 713 pp. Cloth M. 30. Vandenhoeck & Ruprecht, Göttingen, 1924.

Based upon the classic work of late Prof. Dr. Georg Dragendorff, the author at that time, in 1909, at the Pharmaceutical Institute of the University Breslau, wrote the first edition of his book.

Since then he became assistant to that world-wide authority (and honorary member of the A. Ph. A.), Prof. Dr. Ernst Schmidt, and since the latter's death in 1921, his successor as Professor of pharmaceutical chemistry at the University Marburg.

The Introduction and General Part of the work occupy 21 pages and the balance is devoted to the Special Part. This is divided into I. Inorganic Poisons which are cleverly separated into four groups, the second of which is Phosphorus and the fourth comprises the Heavy Metals. Part II. treats the Organic Poisons, divided into Volatile and Non-Volatile Poisons. The latter are again separated into Amido-Poisons and Amido-free Poisons.

The excellent work furthermore contains an Appendix which contains the following important subjects: Systematic Analysis for the Detection of Organic Poisons; Ten Tables for same including Melting Points and Boiling Points; German Poison Laws; Detection of Blood Stains with Blood Spectra Table. The colored table for the qualitative and quantitative tests for Arsenic according to Smith by Beck and Merres is a work of art and shows colorimetrically the presence of As_2O_3 from 40/1000 mg. down to as low as 2/1000 mg. We might add that the chapter on the detection of arsenic occupies 62 pages.

This masterwork by Gadamer is a very valuable contribution to the science of chemical toxicology and forensic chemistry. It is a recognized authority and should also become better known in our country.

OTTO RAUBENHEIMER, Ph. M.

CLINICAL LABORATORY METHODS. By Russell Landram Haden, M. A., M. D., Associate Professor of Medicine, University of Kansas, School of Medicine; Formerly Director of Laboratories, Henry Ford Hospital, Detroit. With 69 Illustrations and 5 Color Plates. 8vo, 294 pp. Cloth, $3.75. C. V. Mosby Company, St. Louis.

The volume is the outgrowth of notebooks used in the development and standardization of the laboratory of a general hospital. The given methods have been thoroughly tried out and found to give accurate results. It is therefore a practical book containing practical methods. Certainly an advantage over other books.

The scope of the work is as follows: Qualitative and Quantitative Analysis of Urine, Analysis of Gastric Juice, Examination of Sputum and of Feces, Qualitative and Quantitative Examination of Blood, Serological Technic, Preparation of Bacteriological Solutions, Stains and Media, General Bacteriological Methods, Miscellaneous Clinical Pathological Examinations, Histological Technic and Examination of Milk and Water.

Each procedure is presented in a simple manner and only one method—a reliable one—is given for each quantitative determination. It is a valuable book for all clinical laboratory workers.

OTTO RAUBENHEIMER, Ph. M.

CHEMICAL CALCULATIONS. By J. S. Long, Ch. E., M. S., Ph. D. and H. V. Anderson, B. Ch. E. 12 mo., 166 pp. Cloth, $1.50. McGraw-Hill Book Co., 370 Seventh Ave., N. Y. City, 1924.

Both authors, professors of chemistry at Lehigh University, have found out that the average college student is weak in arithmetic. Such, by the way, is also true of the student in pharmacy! Therefore this book. From the 14 chapters we want to call attention to the following ones: Conversion of Temperature; Law of Definite and Multiple Proportions; Chemical Equations—Combining Weights—Normal Solutions; Gas Analysis; Electrolysis.

This is not a dry book on chemical calculations but one that is interesting containing detailed explanations, many illustrations and even historical data. We can cheerfully recommend this book to students as well as pharmacists.

OTTO RAUBENHEIMER, Ph. M.

PHYSIKALISCHE RUNDBLICKE. Von Max Planck. 8vo, 116 pp. Verlag von S. Hirzel, Leipzig.

These lectures and papers by the eminent authority, Prof. Dr. Max Planck, of Berlin, deal with different subjects in physics. They were delivered before the Convention of the German Natu-

ralists, The Kaiser Wilhelm Society, The University at Leyden, The Friedrich Wilhelm University at Berlin and The Swedish Academy of Sciences at Stockholm. The last lecture, The Nobel-Vortzag, deals with the Origin and Historical Development of the Quantum Theory, a masterpiece, worth reading and studying, containing also 41 Bibliographic references, valuable to those who wish to investigate further.

The book is a splendid testimonial of the work accomplished by the German scientist.

OTTO RAUBENHEIMER, Ph. M.